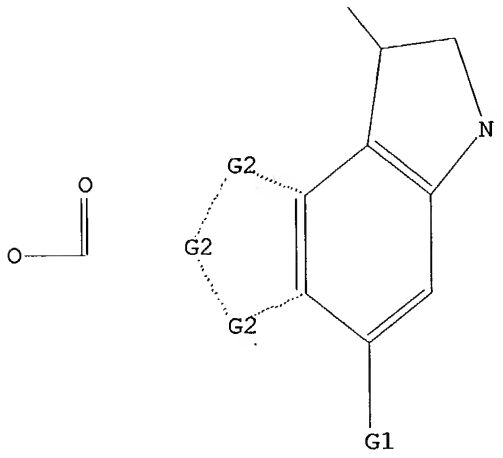
```
=> d his

     (FILE 'HOME' ENTERED AT 14:49:50 ON 22 JUL 2004)

     FILE 'REGISTRY' ENTERED AT 14:49:57 ON 22 JUL 2004
L1              STRUCTURE UPLOADED
L2           50 S L1
L3         1153 S L1 FUL
L4              STRUCTURE UPLOADED
L5            0 S L4 SAM SUB=L3
L6            0 S L4 FUL SUB=L3
L7              STRUCTURE UPLOADED
L8           18 S L7 SAM SUB=L3
L9          401 S L7 FUL SUB=L3
L10         752 S L3 NOT L9
L11             STRUCTURE UPLOADED
L12          18 S L11 FUL SUB=L10
L13         734 S L10 NOT L12

     FILE 'CAPLUS' ENTERED AT 14:56:28 ON 22 JUL 2004
L14         112 S L13

=> d l1; d l4; d l7; d l11; d his; log y
L1 HAS NO ANSWERS
L1              STR
```

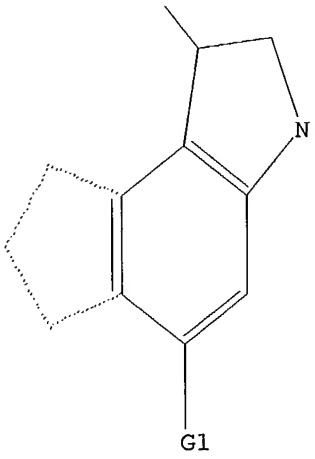


G1 O,S,N

G2 C,N

Structure attributes must be viewed using STN Express query preparation.

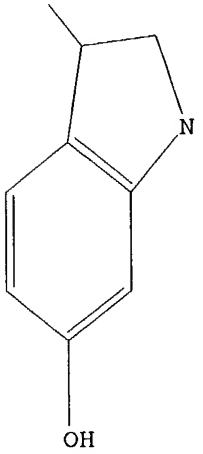
L4 HAS NO ANSWERS
L4 STR



G1 O,S,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

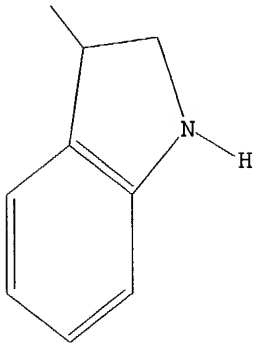
L7 HAS NO ANSWERS
L7 STR



G1 O,S,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

L11 HAS NO ANSWERS
L11 STR



G1 O,S,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 14:49:50 ON 22 JUL 2004)

FILE 'REGISTRY' ENTERED AT 14:49:57 ON 22 JUL 2004

L1		STRUCTURE UPLOADED
L2	50	S L1
L3	1153	S L1 FUL
L4		STRUCTURE UPLOADED
L5	0	S L4 SAM SUB=L3
L6	0	S L4 FUL SUB=L3
L7		STRUCTURE UPLOADED
L8	18	S L7 SAM SUB=L3
L9	401	S L7 FUL SUB=L3
L10	752	S L3 NOT L9
L11		STRUCTURE UPLOADED
L12	18	S L11 FUL SUB=L10
L13	734	S L10 NOT L12

FILE 'CAPLUS' ENTERED AT 14:56:28 ON 22 JUL 2004

L14	112	S L13

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	561.61	831.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-82.32	-82.32

STN INTERNATIONAL LOGOFF AT 14:59:03 ON 22 JUL 2004

L14 ANSWER 1 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:486392 CAPLUS
DN 141:59683
TI Exopolysaccharide micelles for delivery of active molecules
IN Beaudet, Nicolas; Dupont, Claude; Lemieux, Pierre; Simard, Eric; Goyette, Philippe
PA Technologies Biolactis Inc., Can.; INRS (Institut National de Recherche Scientifique)
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

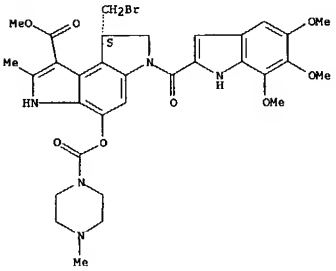
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004050057	A2	20040617	WO 2003-CA1899	20031204

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-430690P P 20021204
AB The present invention relates to a delivery system for delivery of a pharmaceutical active mol. to a patient, the delivery system comprising a population of exopolysaccharide (EPS) micelles, each micelle defining a core for containing the active mol. The active mols. are selected from the group of DNA, RNA, protein, peptide, peptidomimetics, virus, bacteria, neutraceutical products and pharmaceutical agents. It is found that EPS has synergistic effects with some anticancer drugs and can also upregulate expressions of some genes. For example, i.m. injections containing paclitaxel

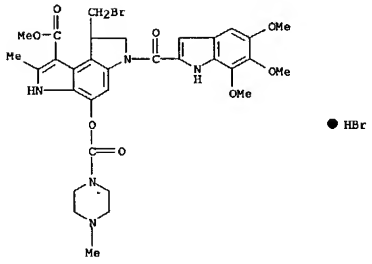
L14 ANSWER 1 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
0.1mM, EPS 0.1% and DMSO 1% had improved antitumor effects than paclitaxel alone.
IT **154009-68-6**, KW-2189
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(micelle compns. containing exopolysaccharides from bacteria and pharmaceutically active agents)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 2 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:69153 CAPLUS
DN 140:246406
TI HnRNP L enhances sensitivity of the cells to KW-2189
AU Taguchi, Fumiko; Kusaba, Hitoshi; Asai, Akira; Iwamoto, Yasuo; Yano, Keiichi; Nakano, Hirofumi; Mizukami, Tamio; Saijo, Nagahiro; Kato, Harubumi; Nishio, Kazuto
CS Pharmacology Division, National Cancer Center Research Institute, Tokyo, Japan
SO International Journal of Cancer (2003), Volume Date 2004, 108(5), 679-685
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Heterogeneous nuclear ribonucleoproteins (hnRNPs) are involved in several RNA-related biol. processes. We demonstrated hnRNP L as a candidate protein of DARP (duocarmycin-DNA adduct recognizing protein) by gel shift assay and amino acid sequencing. Stable transfectants of hnRNP L showed high sensitivity of the cells to the growth inhibitory effect of KW-2189, a duocarmycin derivative in vitro. Immunostaining of hnRNP L demonstrated differential intracellular localization of hnRNP L among human lung cancer cell lines. A transfection study using a series of deletion mutants of hnRNP L fused to indicate that the N-terminal portions of RRM(RNA recognition motif)1, RRM3 and RRM2 are involved in localization of hnRNP L. We identified sequences in these portions that have high homol. with the sequences of known NLS (nuclear localization signal) and NES (nuclear export signal). HnRNP L is a factor that dets. the sensitivities of cancer cells to the minor groove binder, and overexpression and differential intracellular localization of hnRNP L are involved in its function in lung cancer.
IT **148778-32-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hnRNP L (duocarmycin-DNA adduct recognizing protein) enhances sensitivity of cells to KW-2189)
RN 148778-32-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)

L14 ANSWER 2 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



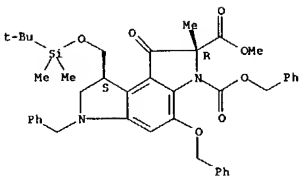
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:361118 CAPLUS
DN 139:85138
TI Total Synthesis of the Duocarmycins
AU Yamada, Ken; Kurokawa, Toshiki; Tokuyama, Hidetoshi; Fukuyama, Tohru
CS Graduate School of Pharmaceutical Sciences, University of Tokyo, Bunkyo,
Tokyo, 113-0033, Japan
SO Journal of the American Chemical Society (2003), 125(22), 6630-6631
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 139:85138
AB The total synthesis of (+)-duocarmycin A and SA through a common indoline
intermediate is described. The key reactions include selective lithiation
of a 2,6-dibromoiodobenzene derivative and diastereoselective addition to a
chiral nitroalkene, copper-mediated aryl amination, and addition of
aryllithium to azlactones.
IT **556038-50-7P 556038-64-3P 556038-65-4P**
556038-66-5P 556038-67-6P
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant
or reagent)
(preparation of (+)-duocarmycin A and SA from a common indoline via
selective lithiation, copper-mediated aryl amination, and
diastereoselective addition)
RN 556038-50-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-6-(phenylmethyl)-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

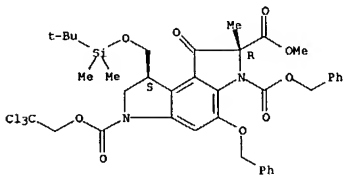
Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 556038-64-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,2,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) 6-(2,2,2-trichloroethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

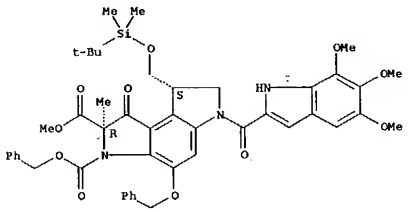
Absolute stereochemistry. Rotation (+).



RN 556038-65-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

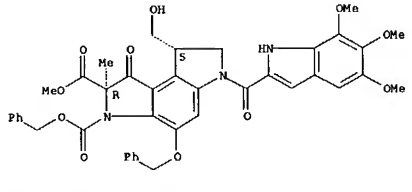
Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 556038-66-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
1,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

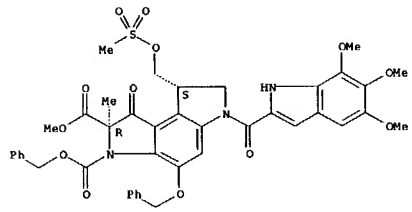
Absolute stereochemistry. Rotation (+).



RN 556038-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(2H)-dicarboxylic acid,
1,6,7,8-tetrahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (2R,8S)- (9CI) (CA INDEX NAME)

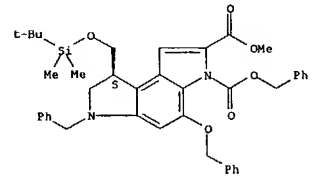
Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **556038-57-4P 556038-69-8P 556038-70-1P**
556038-71-2P 556038-72-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (+)-duocarmycin A and SA from a common indoline via selective lithiation, copper-mediated aryl amination, and diastereoselective addition)
RN 556038-57-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-6-(phenylmethyl)-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

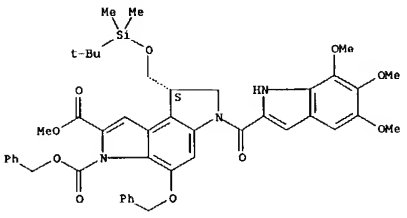
Absolute stereochemistry. Rotation (+).



RN 556038-69-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

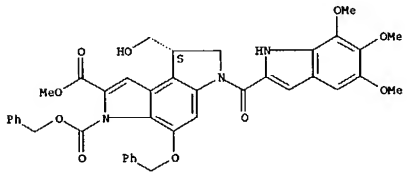
Absolute stereochemistry. Rotation (+).



RN 556038-70-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,

7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

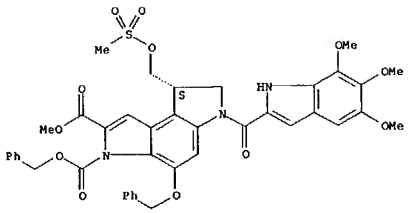


RN 556038-71-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3(6H)-dicarboxylic acid,

7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-methyl 3-(phenylmethyl) ester, (8S)- (9CI) (CA INDEX NAME)

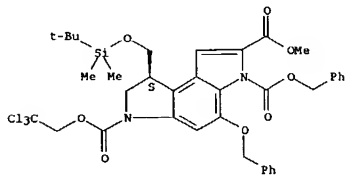
Absolute stereochemistry. Rotation (+).

L14 ANSWER 3 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 556038-72-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-, 2-methyl 3-(phenylmethyl) 6-(2,2,2-trichloroethyl) ester, (8S)- (9CI) (CA INDEX NAME)

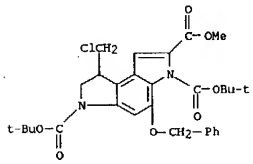
Absolute stereochemistry. Rotation (-).



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

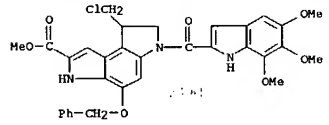
L14 ANSWER 4 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:109220 CAPLUS
DN 139:22032
TI A concise and efficient synthesis of seco-duocarmycin SA
AU Tietze, Lutz F.; Haunert, Frank; Feuerstein, Tim; Herzig, Tobias
CS Institut fur Organische Chemie der Georg August Universitat Gottingen,
Gottingen, 37077, Germany
SO European Journal of Organic Chemistry (2003), (3), 562-566
CODEN: EJOCFK; ISSN: 1434-193X
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 139:22032
AB A short and efficient synthesis of seco-duocarmycin SA

[8-(chloromethyl)-3,6,7,8-tetrahydro-4-hydroxy-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid Me ester], a highly potent cytostatic agent and direct precursor of the natural product duocarmycin SA, has been achieved. Starting from com.
available 2-methoxy-4-nitroaniline the synthetic protocol contains a Fischer indole synthesis to introduce the heterocyclic scaffold and a radical 5-exo-trig cyclization to furnish the (chloromethyl)indoline ring
system as key reactions.
IT **539856-46-7P 539856-47-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(concise and efficient synthesis of seco-duocarmycin SA)
RN 539856-46-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,3,6-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 3,6-bis(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 539856-47-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 4 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:927432 CAPLUS

DN 138:4470

TI Preparation of duocarmycin analogs as potent cytotoxins

IN Ng, Howard P.; McGee, Danny P. C.; Wu, Guoxian; Li, Zhihong; Gangwar, Sanjeev; Saunders, Oliver L.; Martichonok, Valeri; Astafieva, Irina; Moore, Jimmie; Yarranton, Geoffrey Thomas; King, David J.; Boyd, Sharon; Lobl, Thomas J.

PA Coulter Pharmaceutical, Inc., A Wholly Owned Subsidiary of Corixa Corporation, USA

SO PCT Int. Appl., 118 pp.
CODEN: PIXXD2

DT Patent

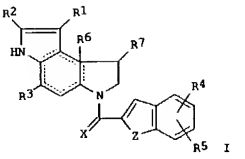
LA English

FAN.CNT 2

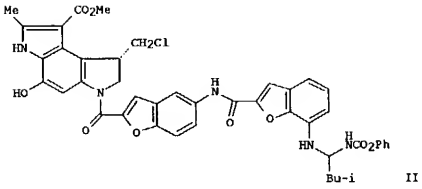
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002096910	A1	20021205	WO 2002-US17210	20020531
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003050331	A1	20030313	US 2002-160972	20020531
	US 2003064984	A1	20030403	US 2002-161234	20020531
	US 2003073852	A1	20030417	US 2002-161233	20020531
	EP 1434778	A1	20040707	EP 2002-731994	20020531
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2001-295196P	P	20010531		
	US 2001-295259P	P	20010531		
	US 2001-295342P	P	20010531		
	US 2001-304908P	P	20010711		
	WO 2002-US17210	W	20020531		

OS MARPAT 138:4470

GI



I



II

AB Duocarmycin analogs I [X, Z = O, S, or imino; R1 = H, (un)substituted alkyl, carboxylic acid, ester, or amide; R2 = H, (un)subsituted alkyl; R3 = :O, OH or derivative; R4, R5 = H, (un)substituted alkyl, (hetero)aryl, heterocycloalkyl, halo, NO2, NR15R16, NCOR15, O2CNR15R16, OCO2R15, COR5, OR15, where R15 and R16 = H, (un)substituted (hetero)alkyl, (hetero)aryl, heterocycloalkyl, or peptidyl or NR15R16 = (un)substituted 4-6 membered heterocycloalkyl; R6 = a single bond; R7 = CH2-X, where X is a leaving group; or R6 and R7 may form a cyclopropyl ring] were prepared as potent cytotoxins. Peptidyl and disulfide linkers are cleaved in vivo. The linkers are of use in forming prodrugs and conjugates of the cytotoxins of the invention as well as other diagnostic and therapeutic moieties. Thus, compound II was prepared via acylation of the 5-amino-2-benzoyl intermediate.

Compds. I generally have an IC50 value in a proliferation assay of .apprx. 1-100 nM, preferably .apprx. 10-10 nM.

IT 477207-70-8P 477207-71-9P 477207-72-0P
477207-73-1P 477207-74-2P 477207-75-3P
477207-76-4P 477207-77-5P 477207-78-6P
477207-79-7P 477207-80-0P 477207-81-1P
477207-82-2P 477207-83-3P 477207-84-4P
477207-85-5P 477207-86-6P 477207-87-7P
477207-96-8P 477207-97-9P 477207-99-1P
477208-00-7P 477208-05-2P 477208-07-4P
477208-10-9P 477208-12-1P 477208-13-2P
477208-14-3P 477208-18-7P 477208-21-2P
477208-24-5P 477208-25-6P 477208-26-7P
477208-27-8P 477208-28-9P 477208-34-7P
477208-39-2P 477208-40-5P 477208-43-8P
477208-44-9P 477208-45-0P 477208-46-1P
477208-47-2P 477208-48-3P 477208-49-4P
477208-50-7P 477208-51-8P 477208-52-9P
477208-53-0P 477208-54-1P 477208-56-3P
477208-57-4P 477208-58-5P 477208-60-9P
477208-61-0P 477208-62-1P 477208-63-2P
477208-65-4P 477208-69-8P 477208-70-1P
477208-71-2P 477208-75-6P 477208-79-0P
477208-84-7P 477208-88-1P 477208-89-2P
477208-90-5P 477208-91-6P 477208-94-9P
477209-15-7P 477209-20-4P 477209-21-5P
477209-23-7P 477209-24-8P 477209-25-9P
477209-26-0P 477209-27-1P 477209-28-2P
477209-32-8P 477209-33-9P 477209-34-0P
477209-35-1P 477209-36-2P 477209-37-3P
477209-38-4P 477209-39-5P 477209-40-8P
477209-41-9P 477209-42-0P 477209-43-1P
477209-44-2P 477209-45-3P 477209-47-5P
477209-48-6P 477209-49-7P 477209-50-0P
477209-51-1P 477209-52-2P 477209-54-4P
477209-59-9P 477209-60-2P 477209-61-3P
477209-62-4P 477209-63-5P 477209-65-7P
477209-66-8P 477209-69-1P 477209-70-4P
477209-71-5P 477209-75-9P 477209-76-0P
477209-77-1P 477209-78-2P 477209-79-3P
477209-80-6P 477209-81-7P 477209-82-8P
477209-83-9P 477209-84-0P 477209-85-1P
477209-86-2P 477209-87-3P 477209-88-4P
477209-89-5P 477209-90-8P 477209-91-9P
477209-92-0P 477209-93-1P 477209-94-2P
477209-95-3P 477209-96-4P 477209-97-5P
477209-98-6P 477209-99-7P 477210-00-7P
477210-01-8P 477210-02-9P 477210-03-0P
477210-04-1P 477210-05-2P 477210-06-3P
477210-07-4P 477210-08-5P 477210-09-6P
477210-10-9P 477210-11-0P 477210-12-1P
477210-13-2P 477210-14-3P 477210-15-4P
477210-16-5P 477210-17-6P 477210-18-7P
477210-19-8P 477210-20-1P 477210-21-2P
477210-22-3P 477210-23-4P 477210-24-5P

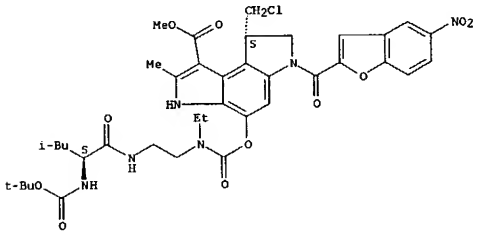
477210-25-6P 477210-26-7P 477210-27-8P
477328-57-7P 477328-58-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of duocarmycin analogs as potent cytotoxins)

RN 477207-70-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(7S)-2-ethyl-11,11-dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

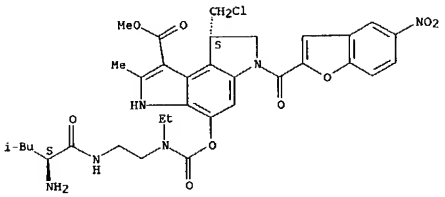


RN 477207-71-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[[(2S)-2-amino-4-methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

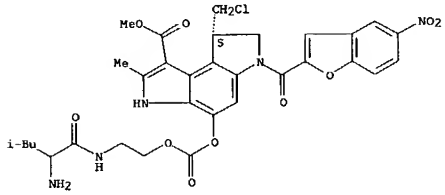
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477207-72-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[2-[(2-amino-4-methyl-

1-oxopentyl)amino]ethoxy]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro
-
2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

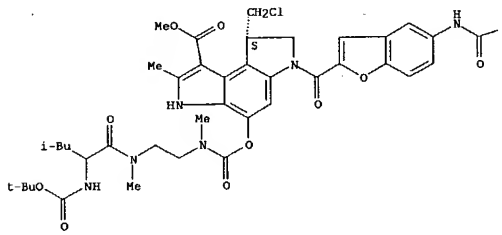


RN 477207-73-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[11,11-
dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-2,10-dioxa-5,8-diazadodec-1-

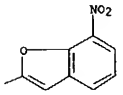
yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



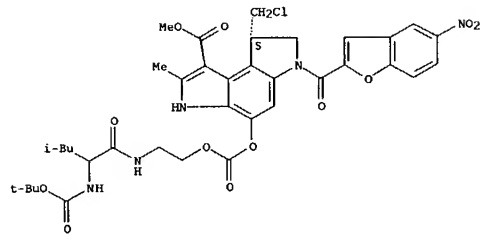
RN 477207-75-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[[2-[(2-amino-4-methyl-

1-oxopentyl)methylamino]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-
3,6,7,8-tetrahydro-2-methyl-6-[[5-[[(7-nitro-2-
benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



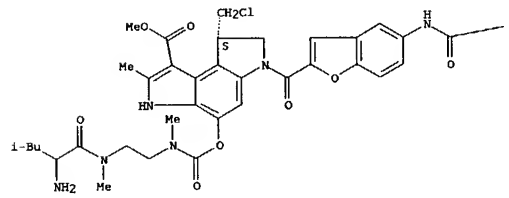
RN 477207-74-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-
tetrahydro-2-methyl-6-[[5-[[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-

benzofuranyl]carbonyl]-4-[[2,5,11,11-tetramethyl-7-(2-methylpropyl)-1,6,9-
trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

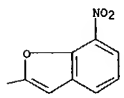
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

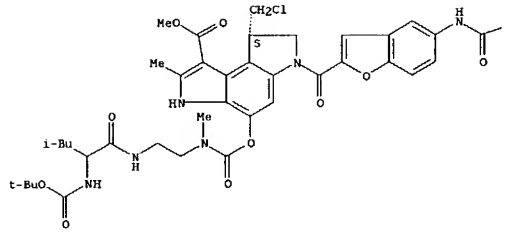


RN 477207-76-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-
tetrahydro-2-methyl-6-[[5-[[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-
benzofuranyl]carbonyl]-4-[[2,11,11-trimethyl-7-(2-methylpropyl)-1,6,9-
trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

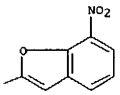
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

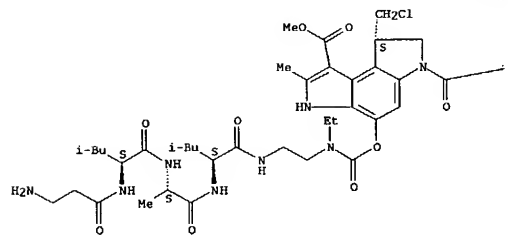


RN 477207-77-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[(2-amino-4-methyl-1-oxopentyl)amino]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

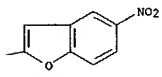
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

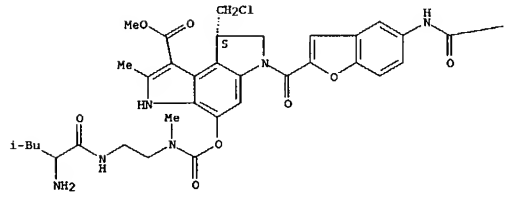


RN 477207-79-7 CAPLUS
CN Glycinamide, L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

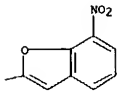
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

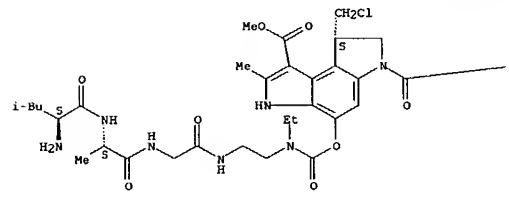


RN 477207-78-6 CAPLUS
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

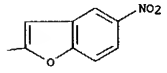
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

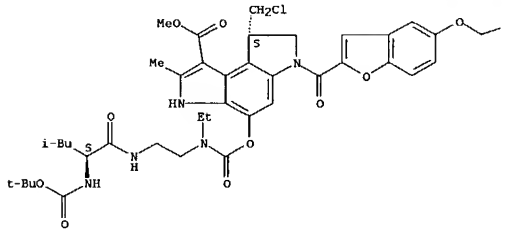


RN 477207-80-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[(7S)-2-ethyl-11,11-dimethyl-7-(2-methylpropyl)-1,6,9-trioxo-10-oxa-2,5,8-triazadodec-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

RN 477207-81-1 CAPLUS
CN L-Leucinamide,
N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-

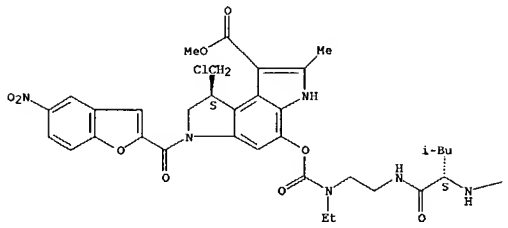
L-alanyl-L-leucyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-1-

(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

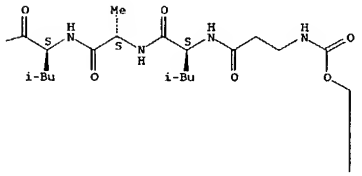
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

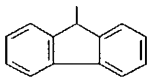


PAGE 1-B



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-B



RN 477207-82-2 CAPLUS
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-L-leucyl-N-[2-[[[[(8S)-8-

(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

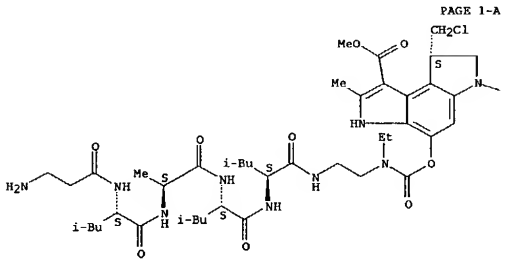
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

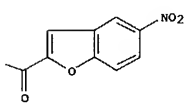
(chloromethyl)-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



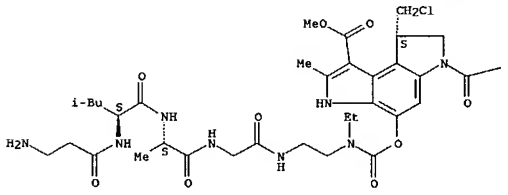
PAGE 1-B



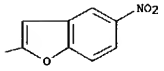
RN 477207-83-3 CAPLUS
CN Glycinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



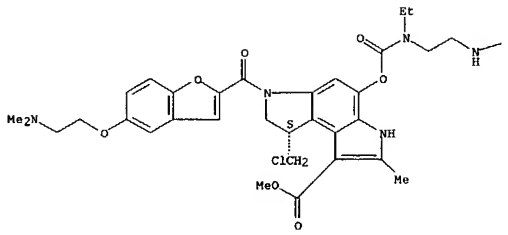
RN 477207-84-4 CAPLUS
CN L-Leucinamide,
N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-

L-alanyl-N-[2-[[[[(8S)-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

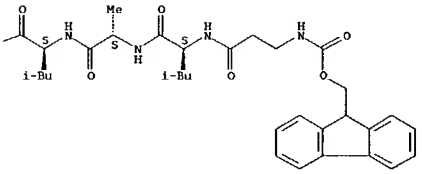
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



RN 477207-85-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[[2-[[(2S)-2-amino-4-

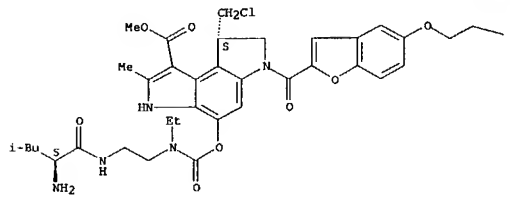
methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-6
-

[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-
2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

RN 477207-86-6 CAPLUS
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[[(8S)-8-

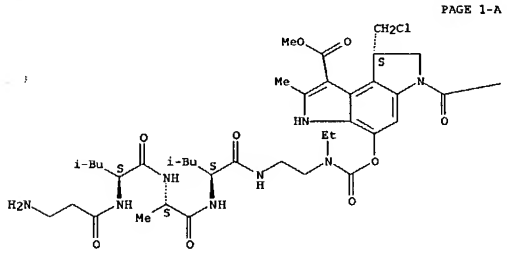
(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-

3,6,7,8-tetrahydro-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-
4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

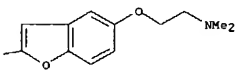
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

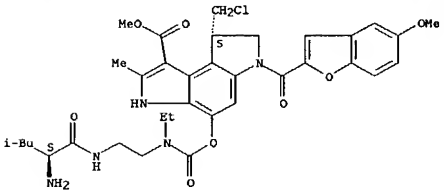


RN 477207-87-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[[2-[[(2S)-2-amino-4-

methyl-1-oxopentyl]amino]ethyl]ethylamino]carbonyl]oxy]-8-(chloromethyl)-
3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

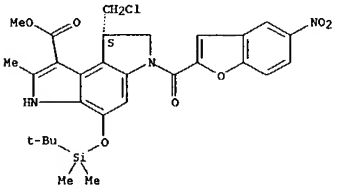
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477207-96-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-
benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

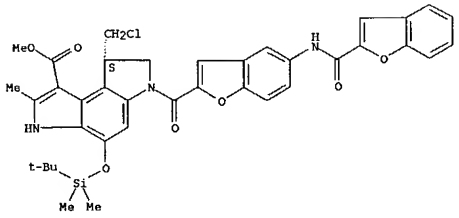


RN 477207-97-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-

benzofuranylcarbonyl)amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

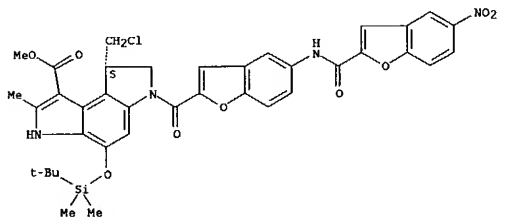
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477207-99-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[(5-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

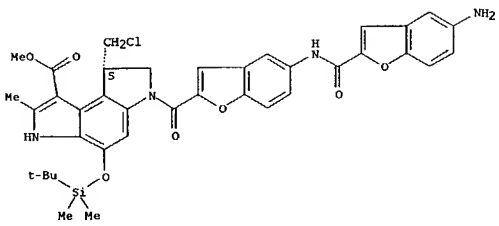
Absolute stereochemistry.



RN 477208-00-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(5-amino-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

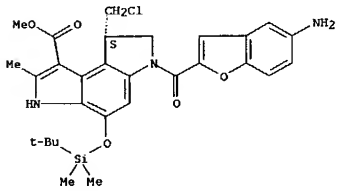
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 477208-05-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

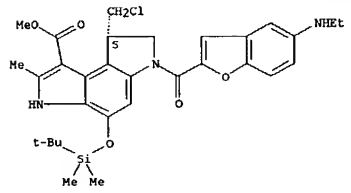
Absolute stereochemistry.



RN 477208-07-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-(ethylamino)-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

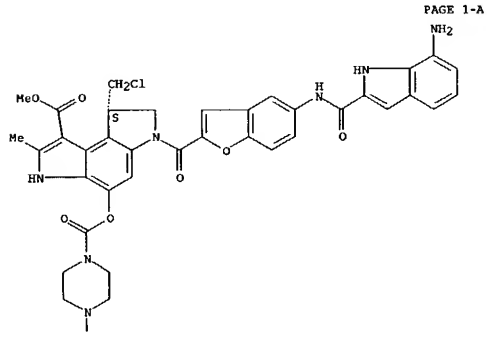
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-10-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(7-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



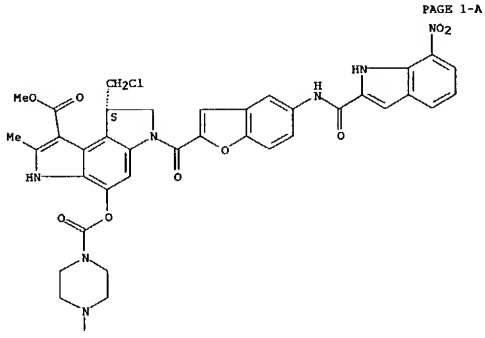
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

RN 477208-12-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[5-[[(7-nitro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

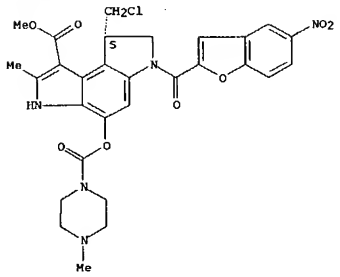
PAGE 1-A



PAGE 2-A

RN 477208-13-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

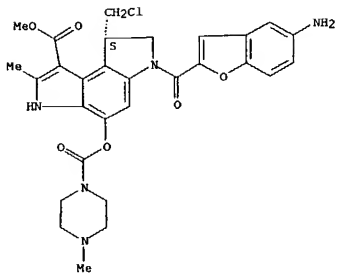


RN 477208-14-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-

benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4
-
methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

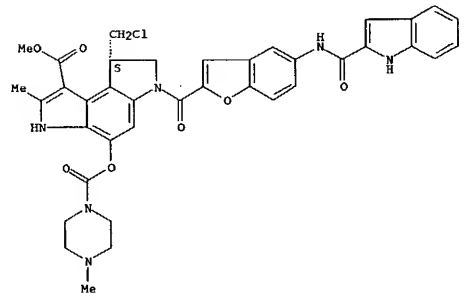


RN 477208-18-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-2-benzofuranyl]carbonyl]-2-
methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



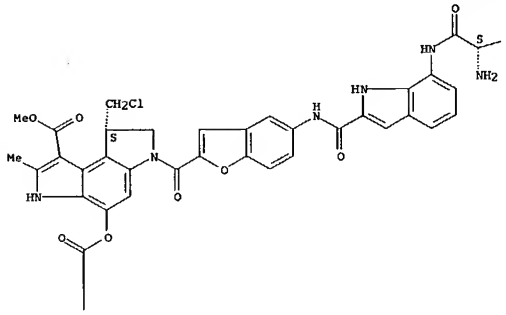
RN 477208-21-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
6-[[5-[[[7-[[(2S)-2-amino-
4-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-

benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4
-
methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

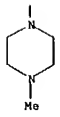
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

PAGE 2-A

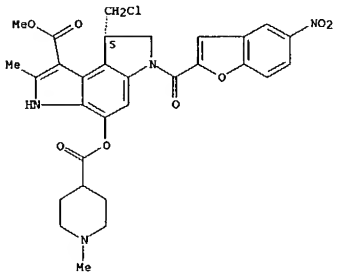


RN 477208-24-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-6-[(5-nitro-
2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

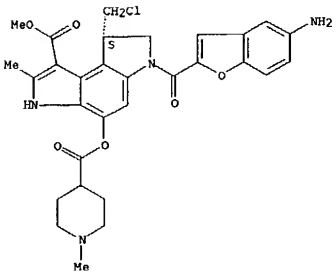
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-25-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(5-amino-2-benzofuranyl)carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

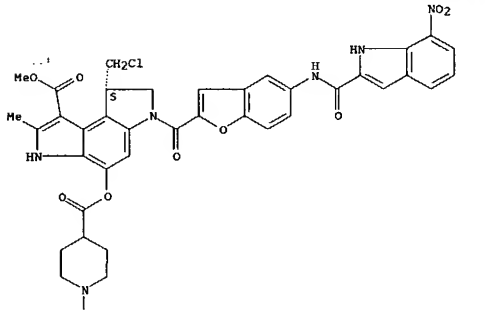


RN 477208-26-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-6-[[5-[[(7-nitro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



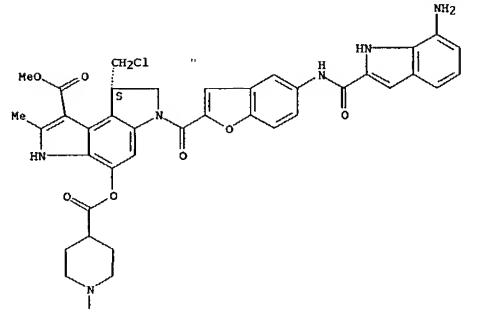
PAGE 2-A

RN 477208-27-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(7-amino-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

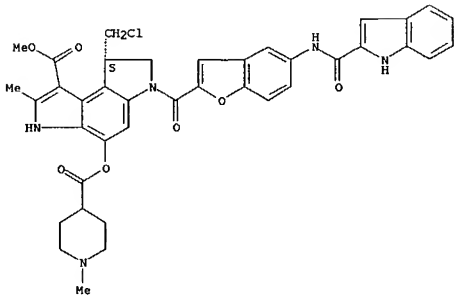


PAGE 2-A

RN 477208-28-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[(1H-indol-2-ylcarbonyl)amino]-2-benzofuranyl]carbonyl]-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

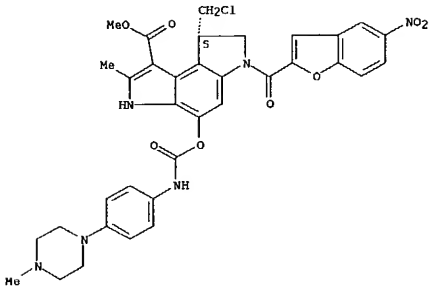


RN 477208-34-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[[[4-(4-methyl-1-piperazinyl)phenyl]amino]carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

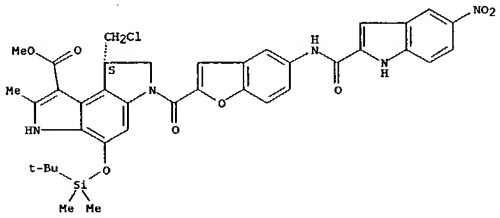
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-39-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[(5-nitro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

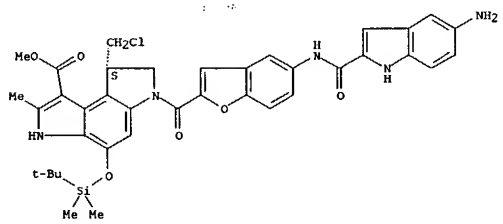


RN 477208-40-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(5-amino-1H-indol-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

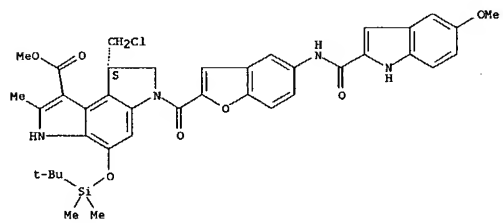
Absolute stereochemistry.



RN 477208-43-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



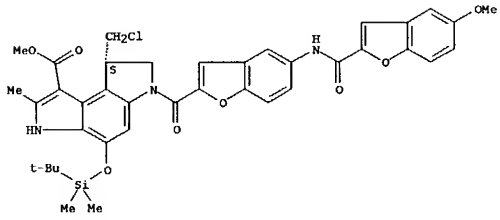
RN 477208-44-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[(5-methoxy-2-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

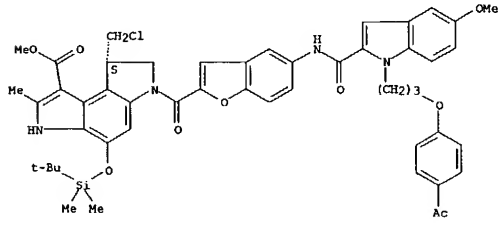
benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477208-45-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-acetylphenoxy)propyl]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

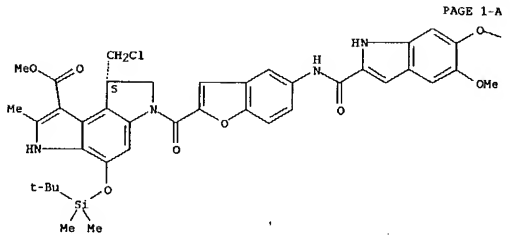


RN 477208-46-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[6-[3-(4-acetylphenoxy)propoxy]-5-methoxy-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

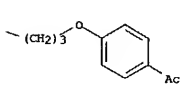
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

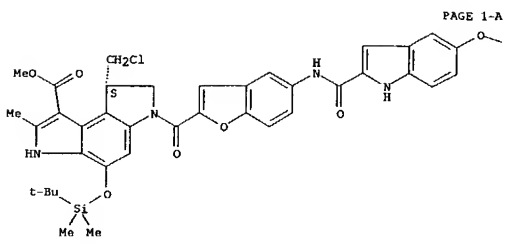


RN 477208-47-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[3-(4-acetylphenoxy)propoxy]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

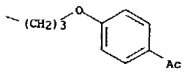
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

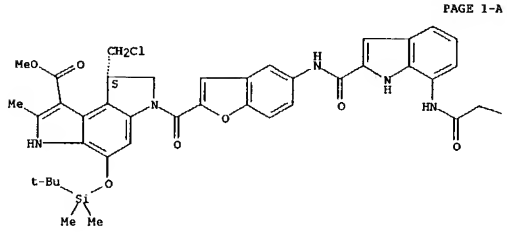


RN 477208-48-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[(4-acetylphenoxy)acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

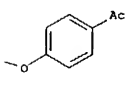
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

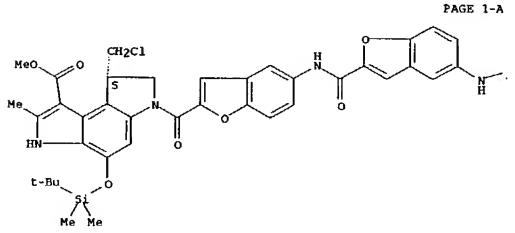


RN 477208-49-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[(4-acetylphenoxy)acetyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

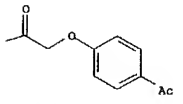
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



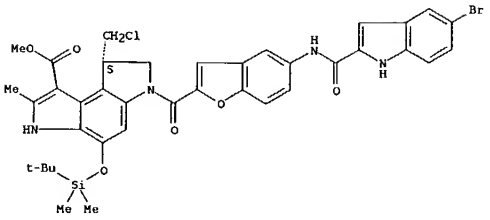
PAGE 1-B



RN 477208-50-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(5-bromo-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

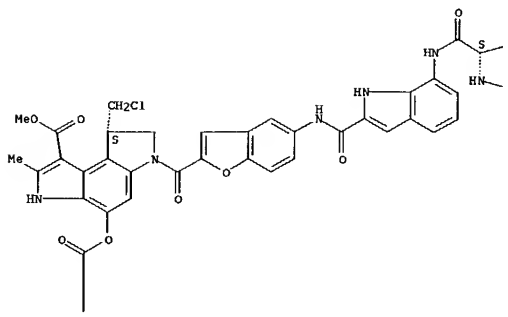


RN 477208-51-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[7-[[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

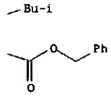
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

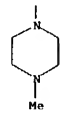


PAGE 1-B



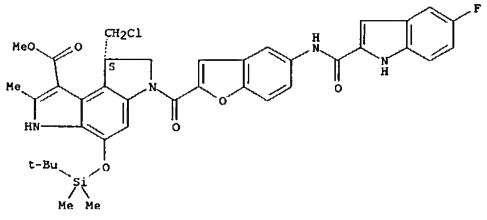
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



RN 477208-52-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

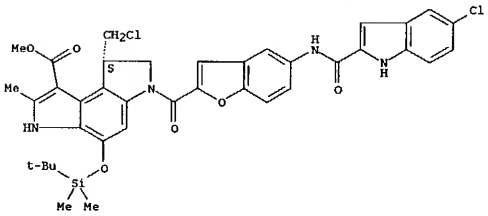
Absolute stereochemistry.



RN 477208-53-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

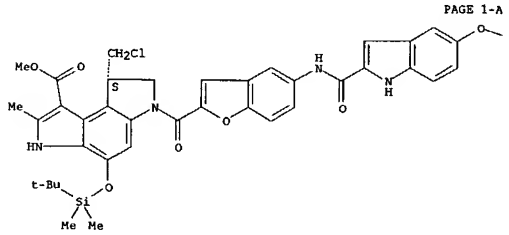
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-54-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[5-(trifluoromethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

RN 477208-56-3 CAPLUS

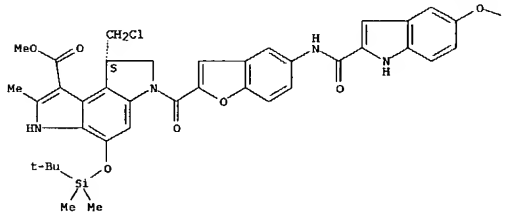
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[5-

(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

RN 477208-57-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[4-

(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

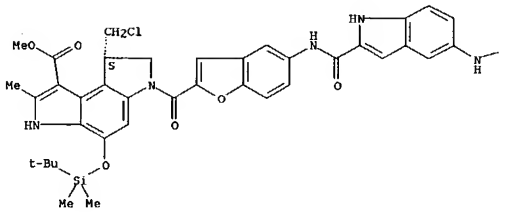
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

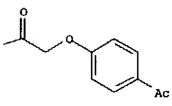
RN 477208-60-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[5-[[(4-
acetylphenoxy)acetyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-
benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

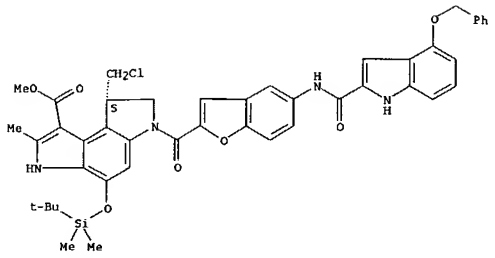


RN 477208-61-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
6-[[5-[[[5-[(2-[[3-(4-
acetylphenoxy)propyl]dithio]-2-methyl-1-oxopropyl]amino]-2-

benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



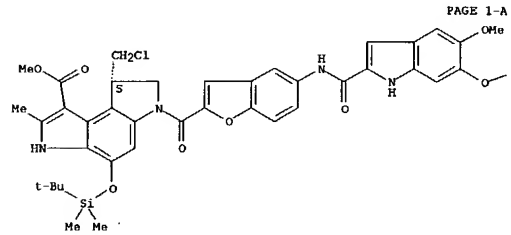
RN 477208-58-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[[5-methoxy-6-

(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-2-
methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

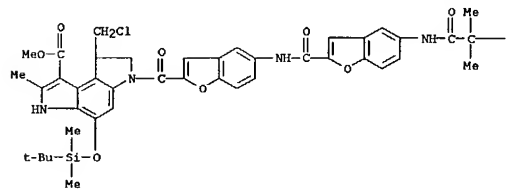
Absolute stereochemistry.

PAGE 1-A

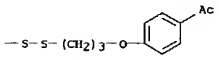


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,
methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



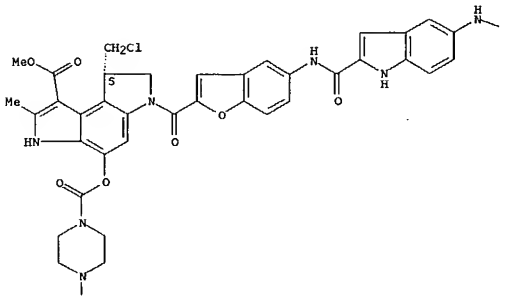
RN 477208-62-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
6-[[5-[[[5-[[(2S)-2-amino-
4-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-

benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-
methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



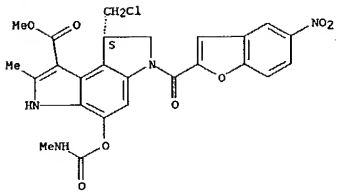
PAGE 1-B

PAGE 2-A

RN 477208-63-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(methylamino)carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

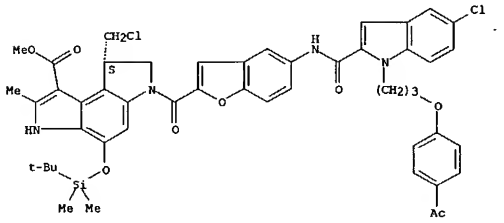
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-65-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[1-[3-(4-acetylphenoxy)propyl]-5-chloro-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

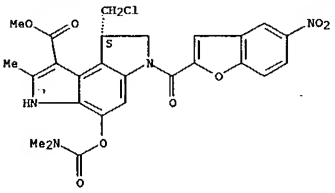
Absolute stereochemistry.



RN 477208-69-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

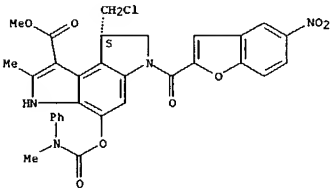
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



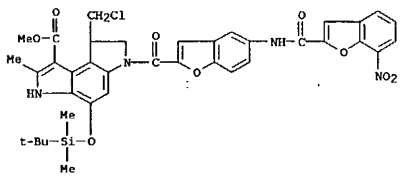
RN 477208-70-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(methylphenylamino)carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



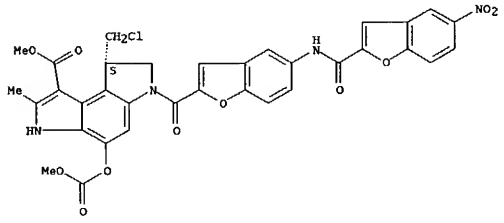
RN 477208-71-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



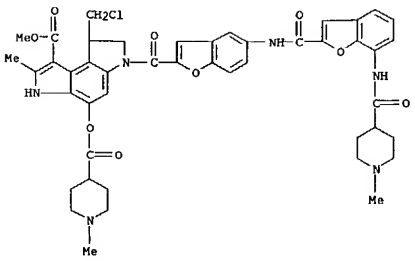
RN 477208-75-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(methoxycarbonyl)oxy]-6-[[5-[[(7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

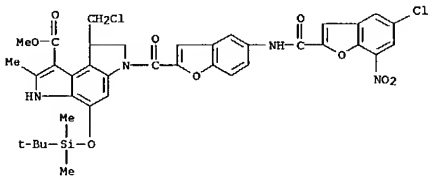


RN 477208-79-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[[5-[[[7-[[(1-methyl-4-piperidinyl)carbonyl]amino]-2-benzofuranyl]carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

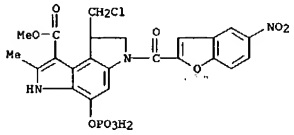


RN 477208-84-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[(5-chloro-7-nitro-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



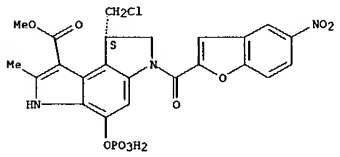
RN 477208-88-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[bis(1,1-dimethylethoxy)phosphinyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477208-91-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-(phosphonooxy)-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

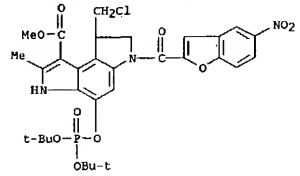
Absolute stereochemistry.



RN 477208-94-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[(7-amino-2-benzofuranyl)carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

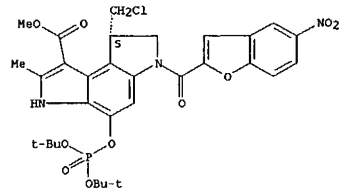
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



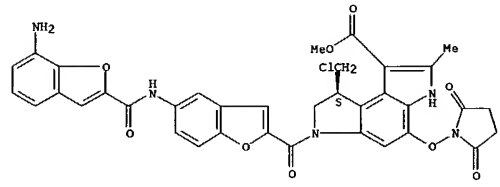
RN 477208-89-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[bis(1,1-dimethylethoxy)phosphinyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



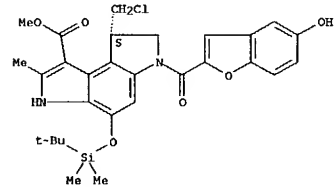
RN 477208-90-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-(phosphonooxy)-, 1-methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-15-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[(5-hydroxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

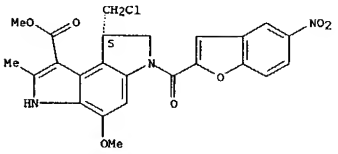
Absolute stereochemistry.



RN 477209-20-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-methoxy-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



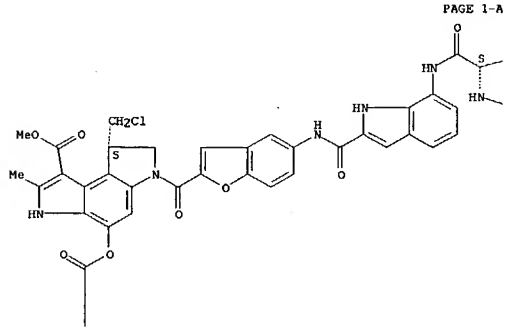
RN 477209-21-5 CAPLUS
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-

(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-

piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

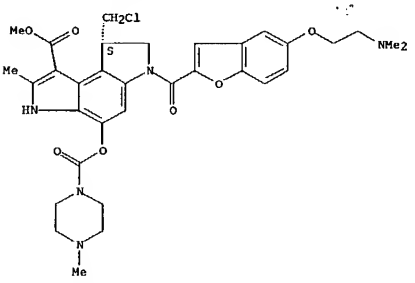
Absolute stereochemistry.

PAGE 1-A



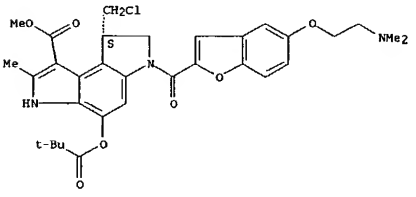
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



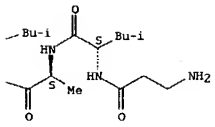
RN 477209-25-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-(2,2-dimethyl-1-oxopropoxy)-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

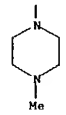


RN 477209-26-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
PAGE 1-B

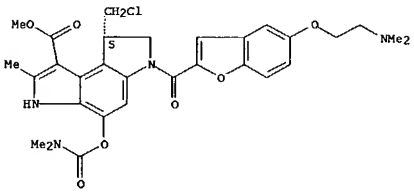


PAGE 2-A



RN 477209-23-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(dimethylamino)carbonyl]oxy]-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)-
(9CI) (CA INDEX NAME)

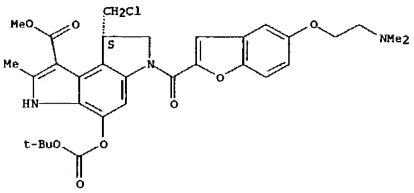
Absolute stereochemistry.



RN 477209-24-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-

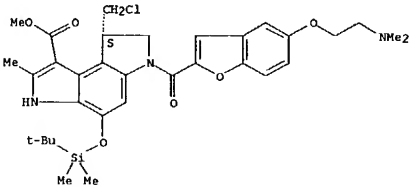
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethoxy)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-27-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

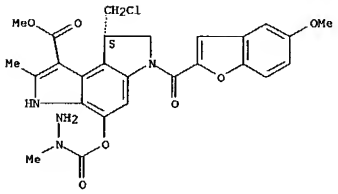
Absolute stereochemistry.



RN 477209-28-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

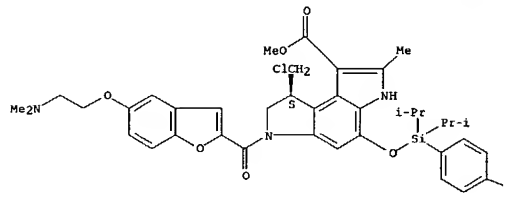
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-32-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-4-[[[4-(methoxymethoxy)phenyl]bis(1-methylethyl)silyl]oxy]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

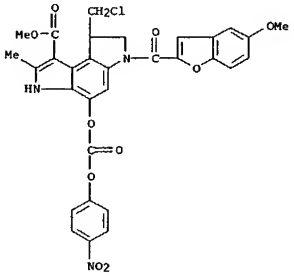
PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

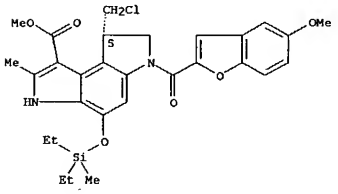
RN 477209-33-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[[(4-nitrophenoxy)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 477209-34-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[(diethylmethylsilyl)oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

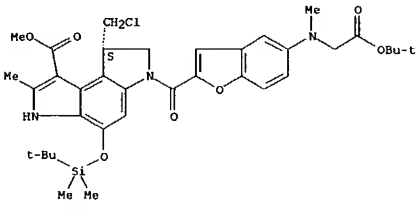
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 477209-35-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[2-(1,1-dimethylethoxy)-2-oxoethyl]methylamino]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

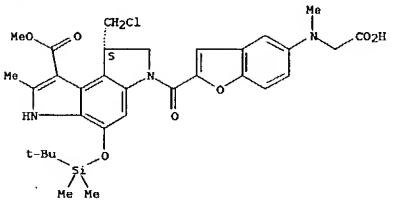
Absolute stereochemistry.



RN 477209-36-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(carboxymethyl)methylamino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

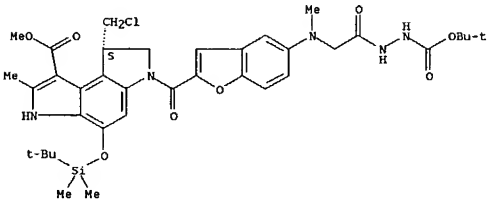
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-37-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[[2-[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl]methylamino]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

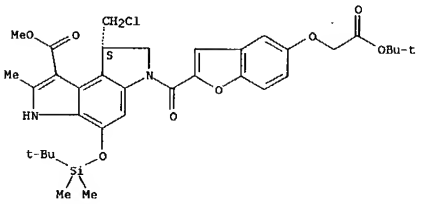
Absolute stereochemistry.



RN 477209-38-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-(1,1-dimethylethoxy)carbonyl]-2-oxoethoxy]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

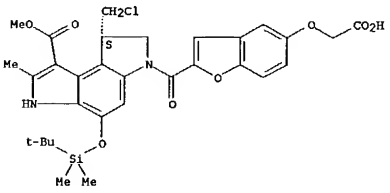
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-39-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-(carboxymethoxy)-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

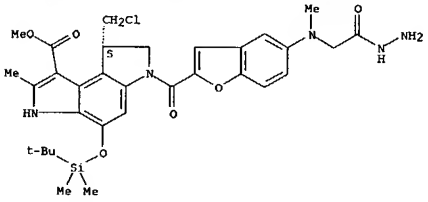
Absolute stereochemistry.



RN 477209-40-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[5-[2-[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethoxy]-2-benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

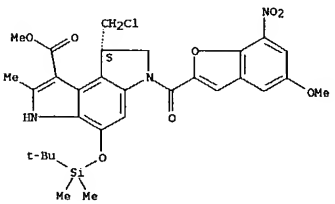
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-43-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-7-nitro-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

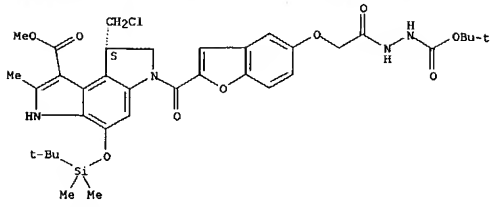
Absolute stereochemistry.



RN 477209-44-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[(7-amino-5-methoxy-2-benzofuranyl)carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

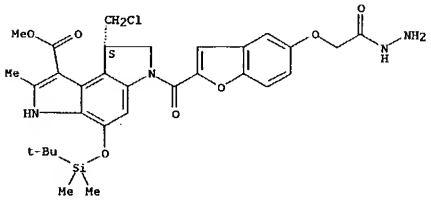
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-41-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-(2-hydrazino-2-oxoethoxy)-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

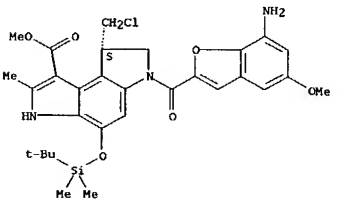
Absolute stereochemistry.



RN 477209-42-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-[[5-[(2-hydrazino-2-oxoethyl)methylamino]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

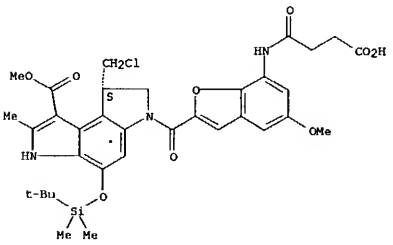
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-45-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[7-[(3-carboxy-1-oxopropoxy)amino]-5-methoxy-2-benzofuranyl]carbonyl]-8-(chloromethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

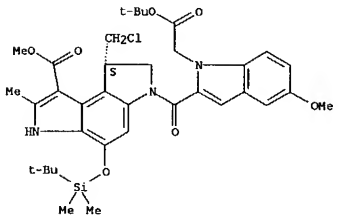
Absolute stereochemistry.



RN 477209-47-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-6-[[1-[2-(1,1-dimethylethoxy)-2-oxoethyl]-5-methoxy-1H-indol-2-yl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

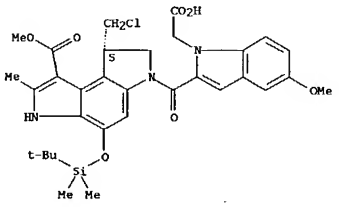
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-48-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
6-[[1-(carboxymethyl)-5-
methoxy-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,
1-methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477209-49-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-6-[[1-[2-

[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl]-5-methoxy-1H-indol
-
2-yl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-
tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

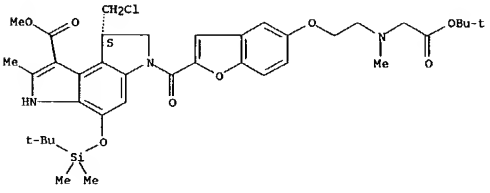
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

RN 477209-51-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-6-[[5-[2-
[[2-(1,1-dimethylethoxy)-2-oxoethyl]methylamino]ethoxy]-2-

benzofuranyl]carbonyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-
tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

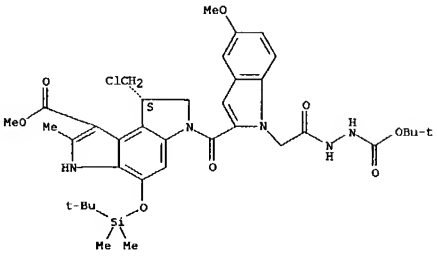


RN 477209-52-2 CAPLUS
CN L-Leucinamide,
N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-
L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-5-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-1,6-dihydro-8-(methoxycarbonyl)-7-
methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-
benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

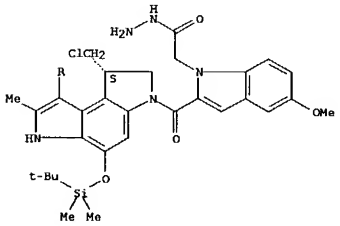


RN 477209-50-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-6-[[1-(2-hydrazino-2-oxoethyl)-5-methoxy-
1H-indol-2-yl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester,
(8S)-
(9CI) (CA INDEX NAME)

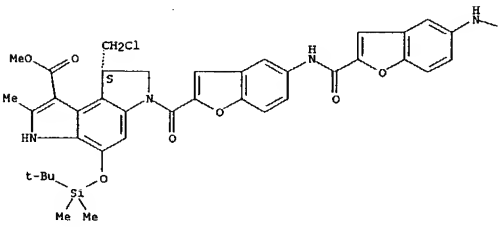
Absolute stereochemistry.

PAGE 1-A

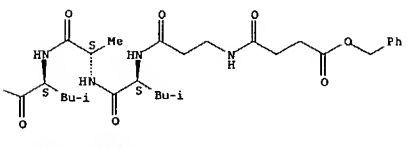


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



RN 477209-54-4 CAPLUS
CN L-Leucinamide,
N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-

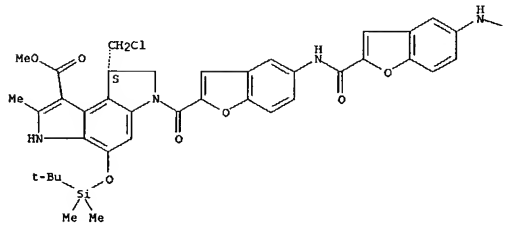
[2-[[[2-[[(1S)-1-(chloromethyl)-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-

1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-
yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI)
(CA
INDEX NAME)

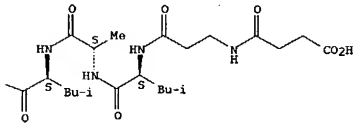
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



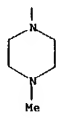
RN 477209-59-9 CAPLUS
CN L-Leucinamide,
N-(5-carboxy-1-oxopentyl)-β-alanyl-L-leucyl-L-alanyl-N-

[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-

[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA
INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



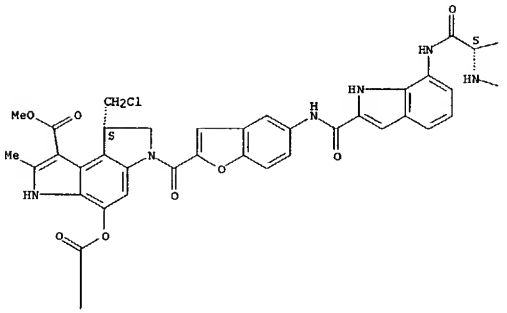
RN 477209-60-2 CAPLUS
CN L-Leucinamide, N-(6-methoxy-1,6-dioxohexyl)-β-alanyl-L-leucyl-L-

alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-
methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-

b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

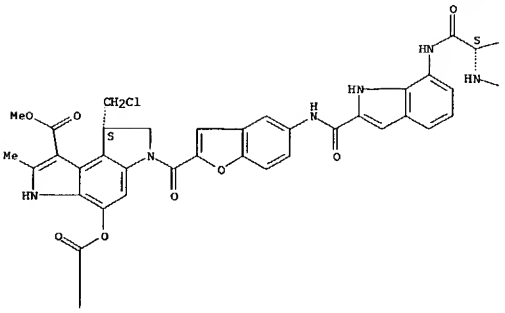
Absolute stereochemistry.

PAGE 1-A

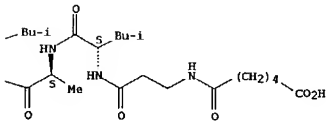


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

PAGE 1-A

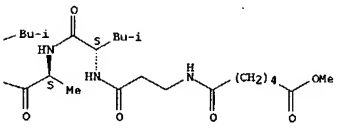


PAGE 1-B

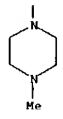


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



PAGE 2-A



RN 477209-61-3 CAPLUS
CN L-Leucinamide,
N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-

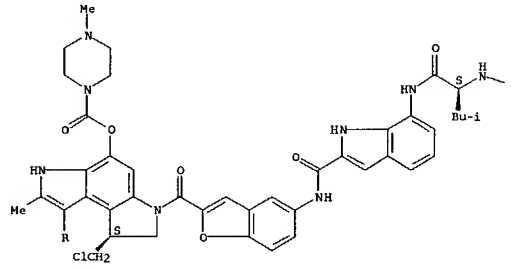
L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-

b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA INDEX NAME)

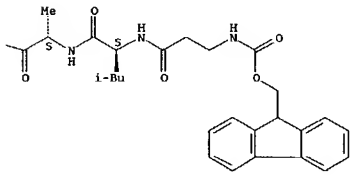
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



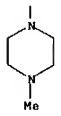
PAGE 1-B



PAGE 2-A

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



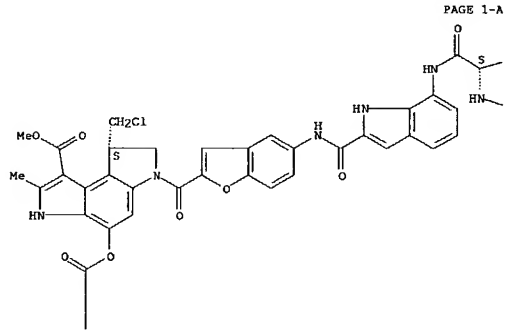
RN 477209-63-5 CAPLUS
CN L-Leucinamide,
N-[1,4-dioxo-4-(phenylmethoxy)butyl]-β-alanyl-L-leucyl-

L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-
7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-

b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

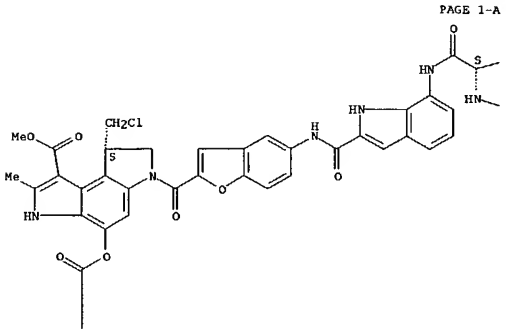
RN 477209-62-4 CAPLUS
CN L-Leucinamide,
N-[1,6-dioxo-6-(phenylmethoxy)hexyl]-β-alanyl-L-leucyl-

L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-
7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-

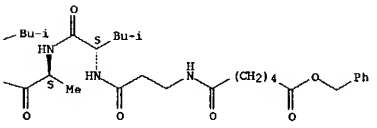
b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-
yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

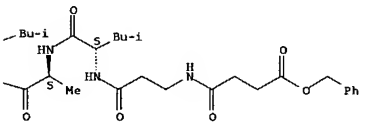


PAGE 1-B

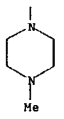


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



PAGE 2-A



RN 477209-65-7 CAPLUS
CN L-Leucinamide,
N-[3-(2,5-dioxo-1-pyrrolidinyl)-1-oxopropyl]-L-leucyl-L-

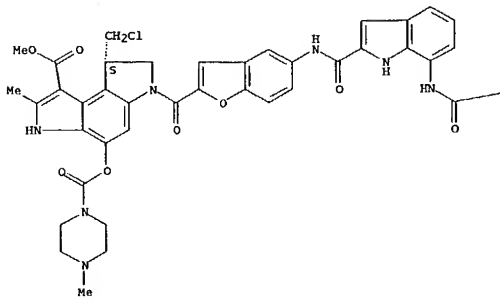
alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-
methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-

b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-
yl]- (9CI) (CA INDEX NAME)

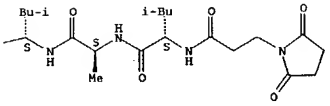
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



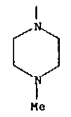
RN 477209-66-8 CAPLUS
CN L-Leucinamide,
N-(3-carboxy-1-oxopropyl)-β-alanyl-L-leucyl-L-alanyl-N-

[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-

[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-1H-indol-7-yl]- (9CI) (CA

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



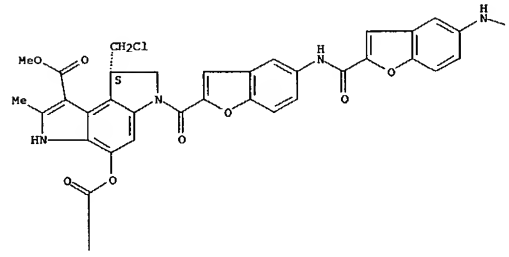
RN 477209-69-1 CAPLUS
CN L-Leucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-

(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-

piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

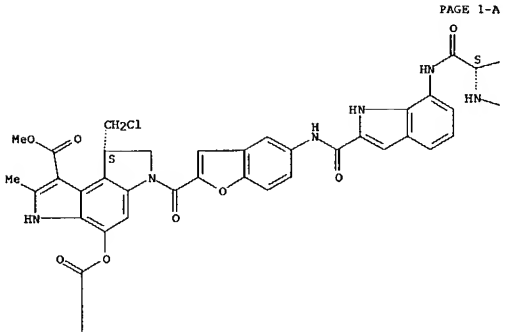
PAGE 1-A



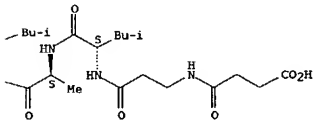
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

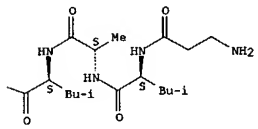


PAGE 1-B



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



PAGE 2-A

RN 477209-70-4 CAPLUS
CN L-Isoleucinamide, β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-

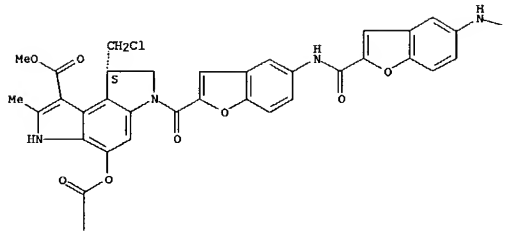
(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-

piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

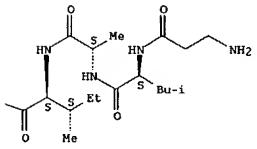
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

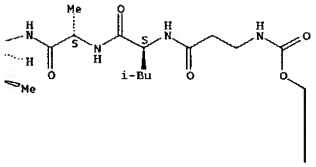


PAGE 1-B

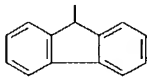


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



PAGE 2-B

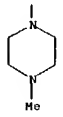


RN 477209-75-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[[[7-[[(2S,3S)-2-amino-3-methyl-1-oxopentyl]amino]-1H-indol-2-yl]carbonyl]amino]-2-benzofuranyl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

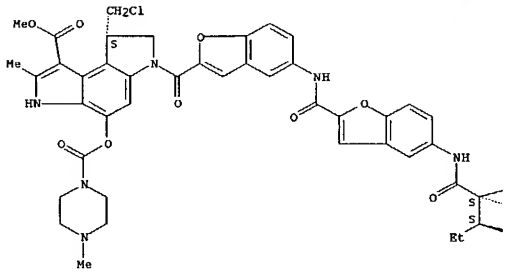
PAGE 2-A



RN 477209-71-5 CAPLUS
CN L-Isoleucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanyl-L-leucyl-L-alanyl-N-[2-[[[2-[[(1S)-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methyl-5-[[(4-methyl-1-piperazinyl)carbonyl]oxy]benzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]amino]carbonyl]-5-benzofuranyl]- (9CI) (CA INDEX NAME)

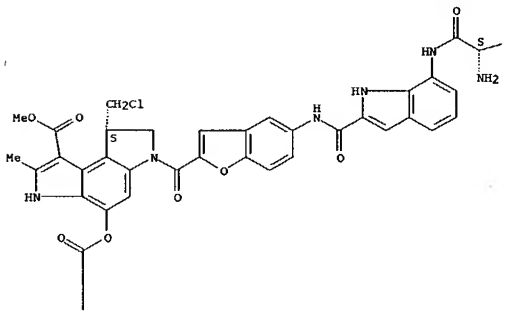
Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

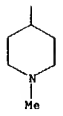
PAGE 1-A



PAGE 1-B

Bu-i

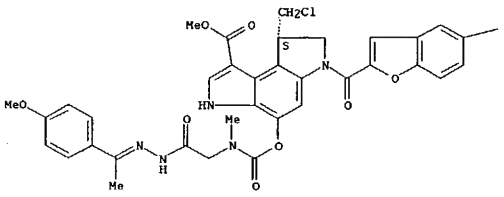
PAGE 2-A



RN 477209-76-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[[2-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

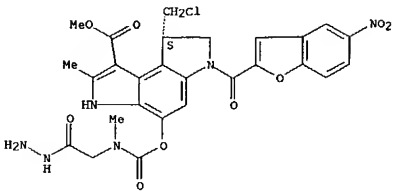
RN 477209-77-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[(2-

hydrazino-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-

6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

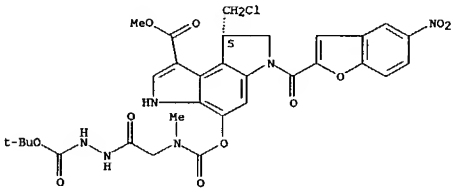
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-78-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[[2-[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

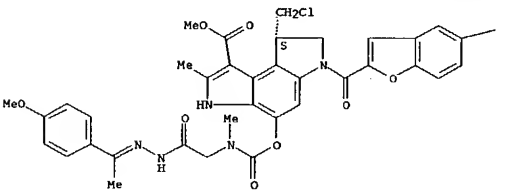


RN 477209-79-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[[2-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



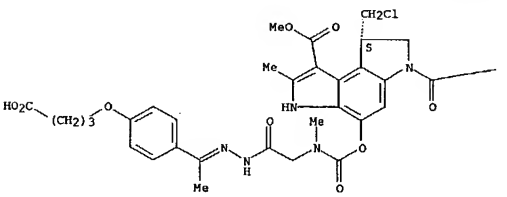
PAGE 1-B

RN 477209-80-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[[1-[4-(3-carboxypropoxy)phenyl]ethylidene]hydrazino]-2-

oxoethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

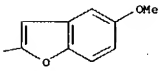
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

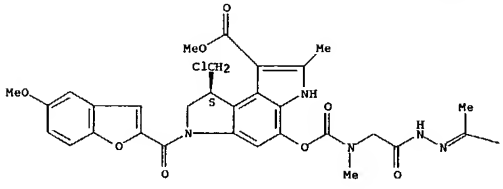


RN 477209-81-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[[2-

[[1-[4-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

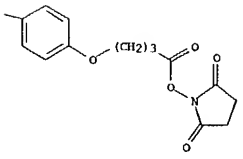
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

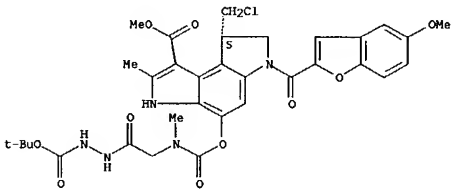
PAGE 1-B



RN 477209-82-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-2-

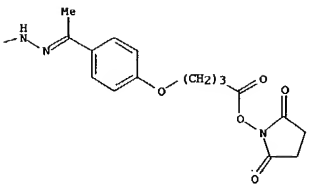
oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-
benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

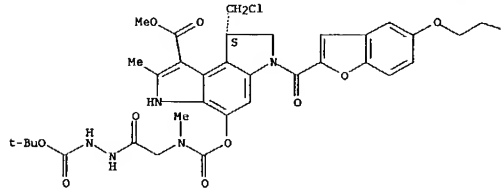


RN 477209-84-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-6-[[5-[2-
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[[2-[2-[(1,1-

dimethylethoxy)carbonyl]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-
3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

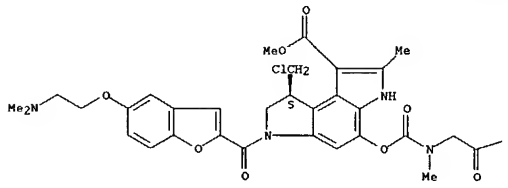
Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



RN 477209-83-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-6-[[5-[2-

(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-4-[[[[2-[(1-[4-[4-[(2,5-
dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-2-
oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-,
methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

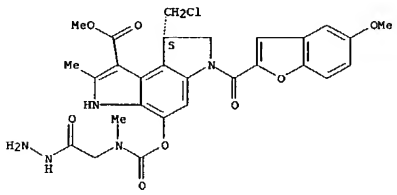
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

RN 477209-85-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[(2-

hydrazino-2-oxoethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-
methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry.



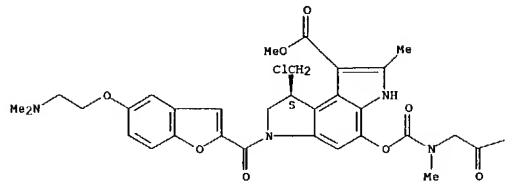
RN 477209-86-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[[1-[4-[4-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]amino]-4-

oxobutoxy]phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy
]-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-
tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

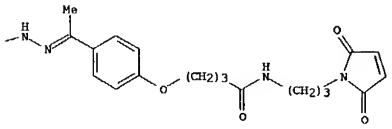
Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



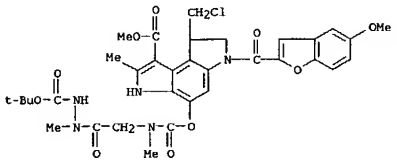
PAGE 1-B



RN 477209-87-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[2-[(1,1-dimethylethoxy)carbonyl]-1-methylhydrazino]-2-

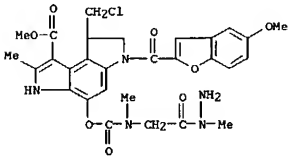
oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-
benzofuranyl)carbonyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-88-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[[[methyl[2-
(1-methylhydrazino)-2-oxoethyl]amino]carbonyl]oxy]-, methyl ester
(9CI)
(CA INDEX NAME)



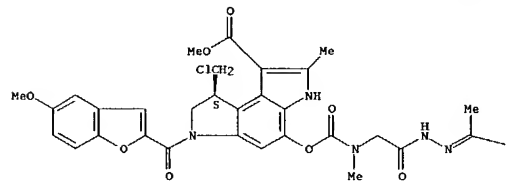
RN 477209-89-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[[1-[4-[4-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]amino]-4-

oxobutoxy]phenyl]ethylidene]hydrazino]-2-oxoethyl]methylamino]carbonyl]oxy
]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl]carbonyl]-2-methyl-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

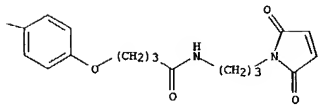
Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



RN 477209-90-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-

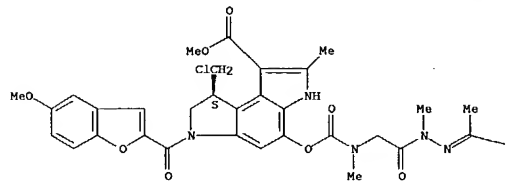
[[1-[4-[4-[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]me

thylhydrazino]-2-oxoethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-
[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

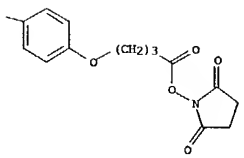
Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



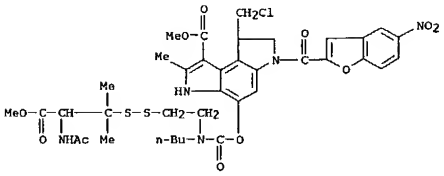
PAGE 1-B



RN 477209-91-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[[2-[[2-(acetylamino)-

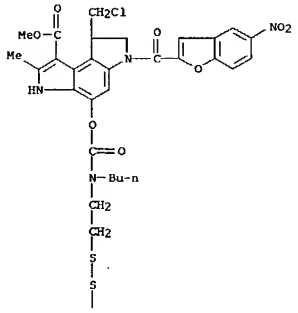
3-methoxy-1,1-dimethyl-3-oxopropyl]dithio]ethyl]butylamino]carbonyl]oxy]-8-
(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-
benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477209-92-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-(2-pyridinyldithio)ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester
(9CI) (CA INDEX NAME)

PAGE 1-A

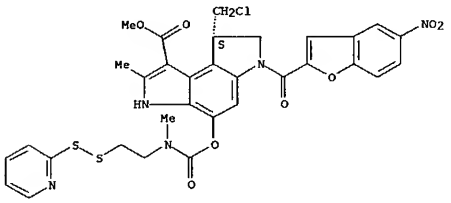


L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

RN 477209-93-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-(2-pyridinyldithio)ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester,
(8S)- (9CI) (CA INDEX NAME)

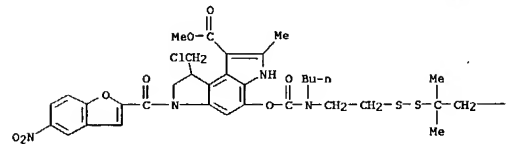
Absolute stereochemistry.



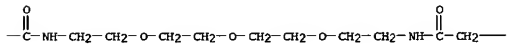
RN 477209-94-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[2-butyl-25-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-7,7-dimethyl-1,9,23-trioxo-13,16,19-trioxa-5,6-dithia-2,10,22-triazapentacos-1-yl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl
ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

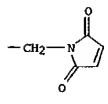
PAGE 1-A



PAGE 1-B



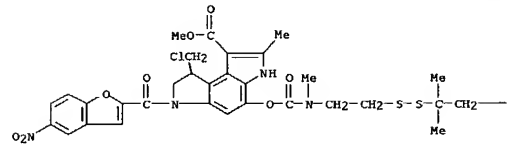
PAGE 1-C



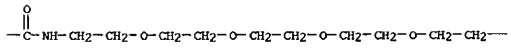
RN 477209-95-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[31-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-2,7,7-trimethyl-1,9,29-trioxo-13,16,19,22,25-pentaoxa-5,6-dithia-2,10,28-triazahentriacont-1-yl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl
ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

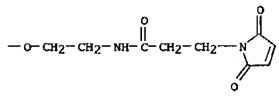
PAGE 1-A



PAGE 1-B



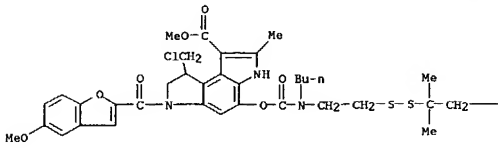
PAGE 1-C



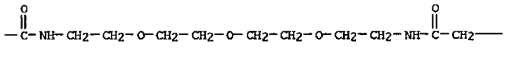
RN 477209-96-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[2-butyl-25-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-7,7-dimethyl-1,9,23-trioxo-13,16,19-trioxa-5,6-dithia-2,10,22-triazapentacos-1-yl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

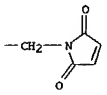
PAGE 1-A



PAGE 1-B



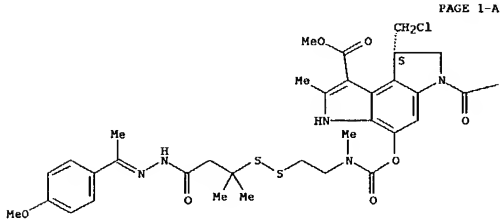
PAGE 1-C



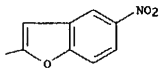
RN 477209-97-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-4-[(2,7,7,14,14-pentamethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-yl)oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

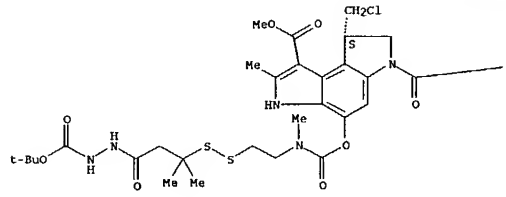


RN 477209-99-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[[2-[[1,1-dimethyl-3-oxo-3-[[1-[4-(3,6,9,12-tetraoxatridec-1-yloxy)phenyl]ethylidene]hydrazino]propyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

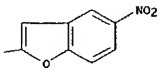
Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

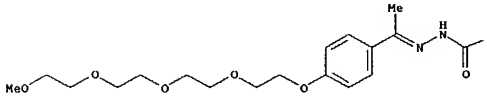


RN 477209-98-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[[2-[[3-[[1-(4-methoxyphenyl)ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

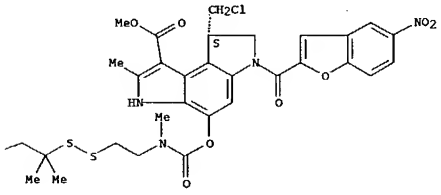
Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

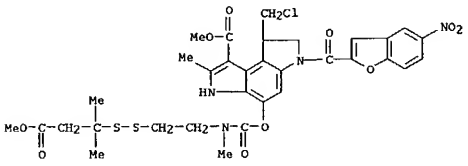


PAGE 1-B



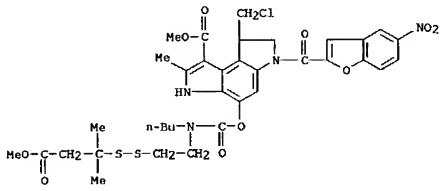
RN 477210-00-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[[2-[(3-methoxy-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]oxy]-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-01-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[butyl[2-[(3-methoxy-

1,1-dimethyl-3-oxopropyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)
-
3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-,
methyl
ester (9CI) (CA INDEX NAME)

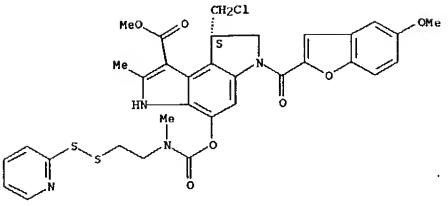


RN 477210-02-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-6-[(5-methoxy-2-benzofuranyl)carbonyl]-4-[[[methyl[2-
(2-pyridinyldithio)ethyl]amino]carbonyl]oxy]-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

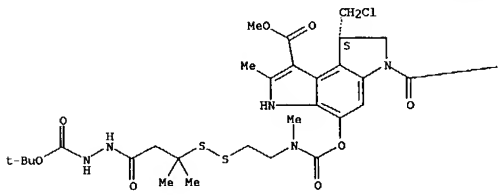


RN 477210-03-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-4-[(2,7,7,14,14-
pentamethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-
yl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

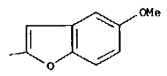
Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

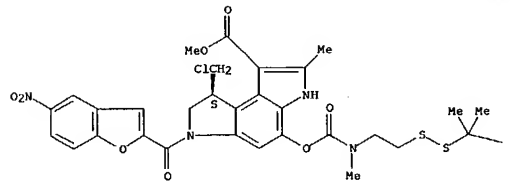


RN 477210-04-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[[3-[[1-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-
yl)phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-

oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-
methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

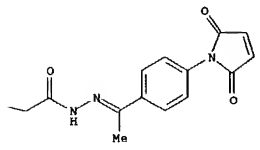
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

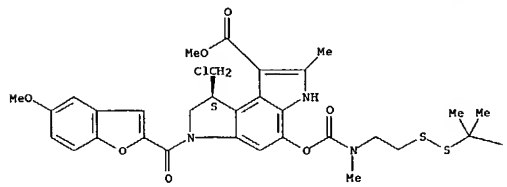


RN 477210-05-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[[3-[[1-[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-
yl)phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-

oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5-
methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

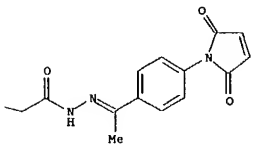
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

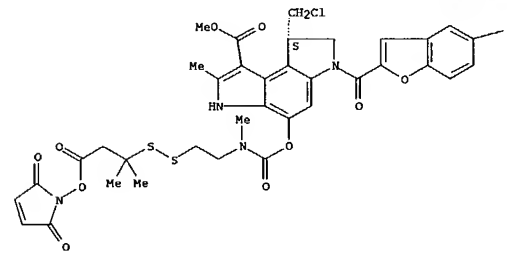
PAGE 1-B



RN 477210-06-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[[3-[(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)oxy]-1,1-dimethyl-3-
oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-6-[[5-[2-
(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-
methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

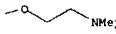
Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

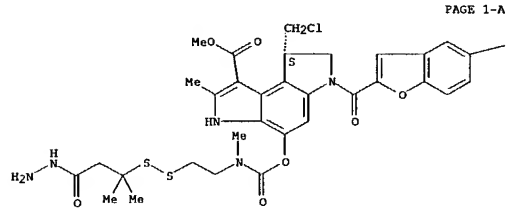
PAGE 1-B



RN 477210-07-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[(3-hydrazino-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]o
xy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



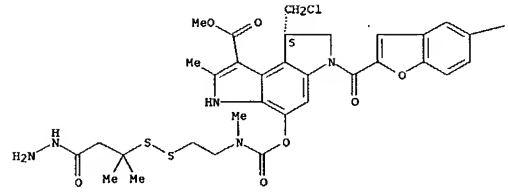
PAGE 1-B

RN 477210-08-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[[2-
[(3-hydrazino-1,1-dimethyl-3-oxopropyl)dithio]ethyl]methylamino]carbonyl]o
xy]-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

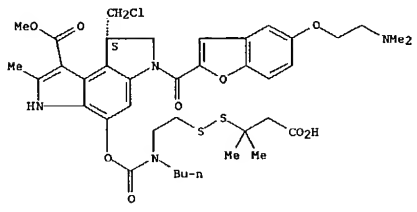
PAGE 1-A



PAGE 1-B

RN 477210-09-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[butyl[2-[(2-carboxy-
1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-
[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-
methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

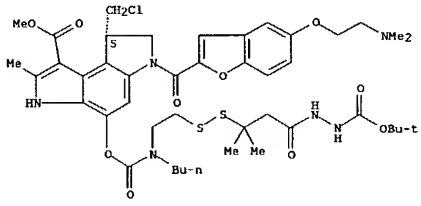
Absolute stereochemistry.



RN 477210-10-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[(2-butyl-7,7,14,14-
tetramethyl-1,9,12-trioxo-13-oxa-5,6-dithia-2,10,11-triazapentadec-1-
yl)oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-
benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester,
(8S)-

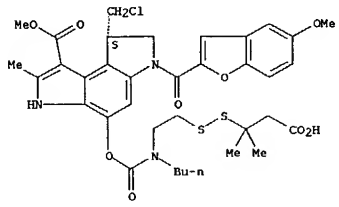
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 477210-11-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[butyl[2-[(2-carboxy-
1,1-dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-
3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-,
1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

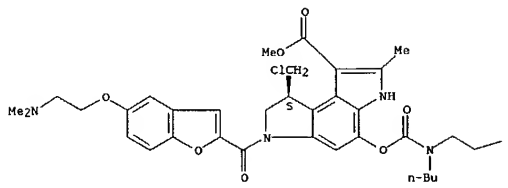


RN 477210-12-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[butyl[2-[[3-[[1-[4-[4-
[(2,5-dioxo-1-pyrrolidinyl)oxy]-4-oxobutoxy]phenyl]ethylidene]hydrazino]-
1,1-dimethyl-3-oxopropyl]dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-
6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-
tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

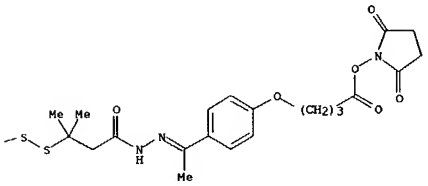
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B

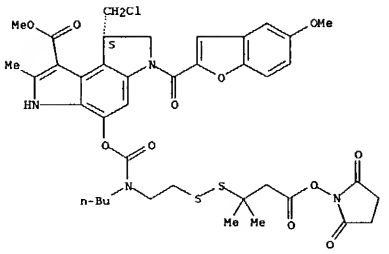


RN 477210-13-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[[3-[(2,5-

dioxo-1-pyrrolidinyl)oxy]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

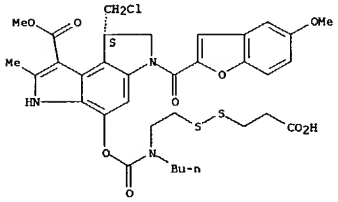
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-14-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-

carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

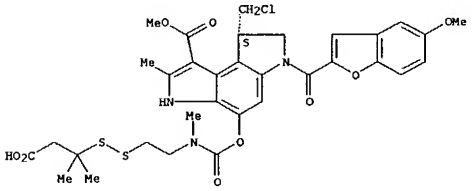
Absolute stereochemistry.



RN 477210-15-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[(2-carboxy-1,1-dimethylethyl)dithio]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

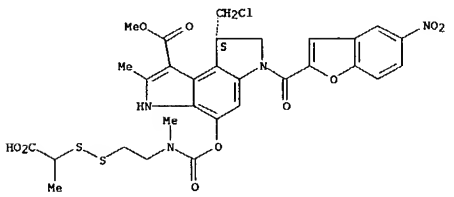
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 477210-16-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[(1-carboxyethyl)dithio]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

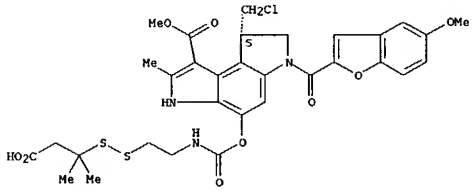


RN 477210-17-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[(2-carboxy-1,1-

dimethylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

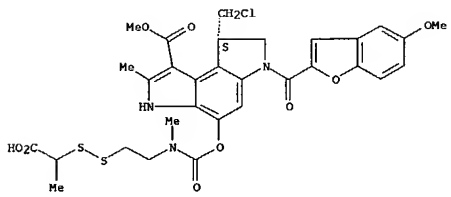
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-18-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[(1-carboxyethyl)dithio]ethyl]methylamino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

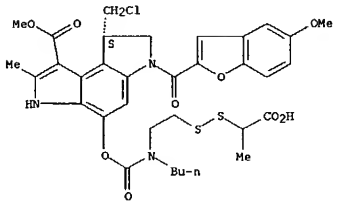


RN 477210-19-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-

carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

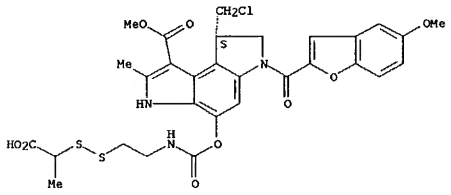
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-20-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[2-[(1-carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

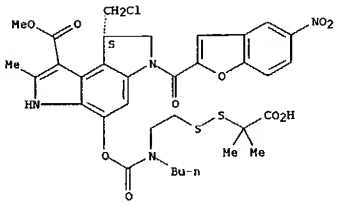
Absolute stereochemistry.



RN 477210-21-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

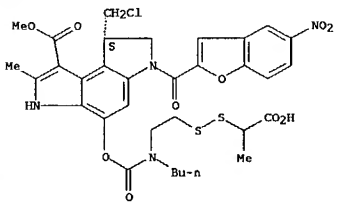
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-22-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(1-carboxyethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

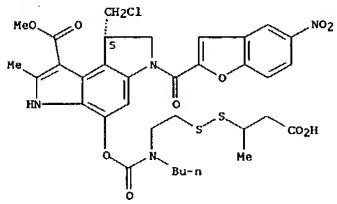
Absolute stereochemistry.



RN 477210-23-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

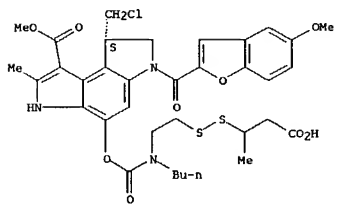
Absolute stereochemistry.

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-24-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-, 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

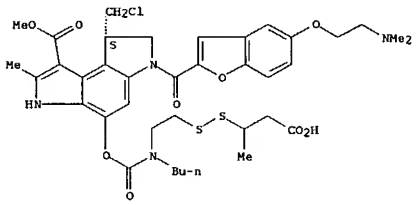
Absolute stereochemistry.



RN 477210-25-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-8-(chloromethyl)-6-[[5-[2-(dimethylamino)ethoxy]-2-benzofuranyl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

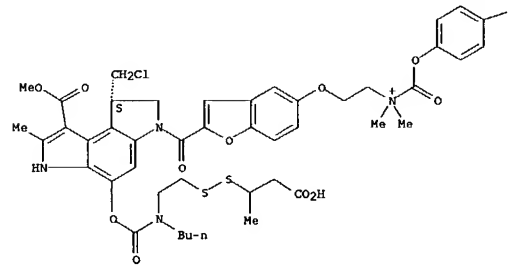
L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 477210-26-7 CAPLUS
CN Ethanaminium, 2-[[2-[[(1S)-5-[[[butyl[2-[(2-carboxy-1-methylethyl)dithio]ethyl]amino]carbonyl]oxy]-1-(chloromethyl)-1,6-dihydro-8-(methoxycarbonyl)-7-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-5-benzofuranyl]oxy]-N,N-dimethyl-N-[(4-nitrophenoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



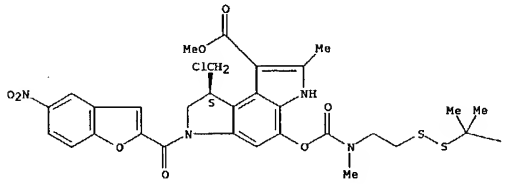
PAGE 1-B

L14 ANSWER 5 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

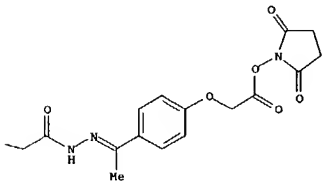
RN 477210-27-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[[2-[[3-[[1-[4-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethoxy]phenyl]ethylidene]hydrazino]-1,1-dimethyl-3-oxopropyl]dithio]ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5-nitro-2-benzofuranyl)carbonyl]-, methyl ester, (8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



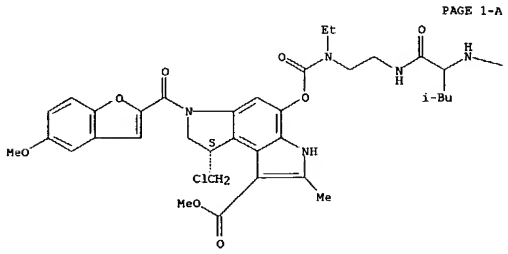
PAGE 1-B



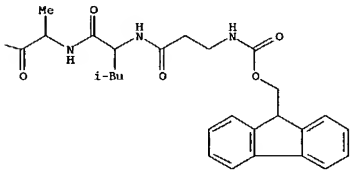
RN 477328-57-7 CAPLUS
CN Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-β-alanylleucylalanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



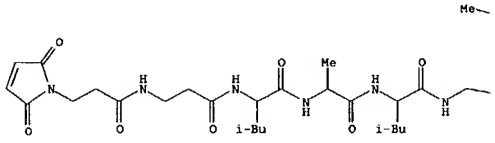
PAGE 1-B



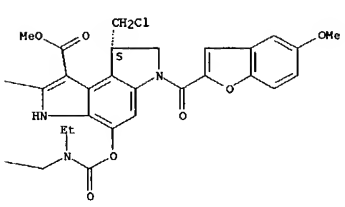
RN 477328-58-8 CAPLUS
CN Leucinamide, N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-β-alanylleucylalanyl-N-[2-[[[[(8S)-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-1-(methoxycarbonyl)-2-methylbenzo[1,2-b:4,3-b']dipyrrol-4-yl]oxy]carbonyl]ethylamino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:755199 CAPLUS
DN 137:284323
TI Enzyme-cleavable prodrug compounds
IN Dubois, Vincent; Fernandez, Anne Marie; Gangwar, Sanjeev; Lewis, Evan; Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Lesley B.; Trouet, Andre; Yarranton, Geoffrey T.
PA Belg.
SO U.S. Pat. Appl. Publ., 86 pp., Cont.-in-part of Appl. No. PCT/US99/30393.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002142955	A1	20021003	US 2001-879442	20010611
WO 2000033888	A2	20000615	WO 1999-US30393	19991210
WO 2000033888	A3	20011108		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

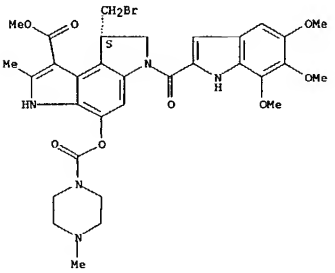
PRAI US 1998-111793P P 19981211
US 1999-119312P P 19990208
WO 1999-US30393 A2 19991210
US 2000-211887P P 20000614
US 2001-290448P P 20010511

OS MARPAT 137:284323
AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide, a stabilizing group and, optionally, a linker group. The prodrug is cleavable by the enzyme Thimet oligopeptidase, or TOP. Also disclosed are methods of designing prodrugs by utilizing TOP-cleavable sequences within the conjugate and methods of treating patients with prodrugs of the invention.
IT **154889-68-6**, KW-2189
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thimet oligopeptidase-cleavable prodrug compds.)
RN 154889-68-6 CAPLUS

L14 ANSWER 6 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 7 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:157495 CAPLUS
DN 136:205412
TI Oligopeptide-based prodrugs activated by plasmin and their use in cancer chemotherapy
IN Trouet, Andre; Dubois, Vincent; Passioukov, Alexandre
PA Coulter Pharmaceutical, Inc., USA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

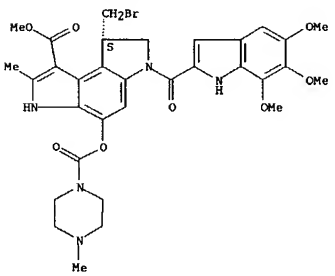
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002015700	A1	20020228	WO 2001-US26476	20010823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001086727	A5	20020304	AU 2001-86727	20010823
PRAI US 2000-227686P	P	20000824		
WO 2001-US26476	W	20010823		

OS MARPAT 136:205412
AB A prodrug, cleavable by plasmin, comprises a therapeutic agent capable of entering a target cell, e.g., a tumor or inflammatory cell, an oligopeptide having a plasmin peptide substrate of 2-4 amino acids and mono- or di-peptide linkage, a stabilizing group and, optionally, a linker group. Also disclosed are methods of making and using the prodrug compds.
For example, the activity of D-Ala-Leu-Lys-Leu-Leu-doxorubicin (I) (preparation given) was evaluated in the B16-B16 murine melanoma model. The mice receiving the prodrug did not show any important weight loss during the experiment and no clin. signs of toxicity were observed At the same time, the drug had a marked effect on the metastatic growth. At 34.5 μmol/kg, I reduced the spread of lung metastases with a decrease of the ratio of the surface

L14 ANSWER 7 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
occupied by B16-B16 colonies to the non-affected one to 8.2±1.8% (P<0.01), compared to 45.7±12.6% and 44.0±6.3% for non-treated and doxorubicin (5.2 μmol/kg)-treated animals. The same prodrug at 69.0 μmol/kg provided 1.5±0.6% of surface affected.
IT **154889-68-6**, KW-2189
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptide-based prodrugs activated by plasmin for chemotherapy)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:10314 CAPLUS
DN 136:86054
TI Tripeptide prodrug compounds
IN Bebbington, Christopher R.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew H.; Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.
PA Corixa Corporation, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

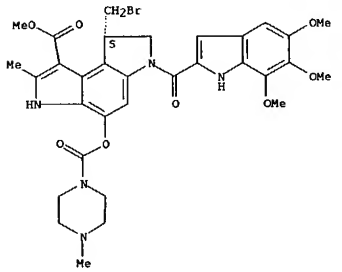
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002000263	A2	20020103	WO 2001-US40925	20010611
WO 2002000263	A3	20020815		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1294403	A2	20030326	EP 2001-942249	20010611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501875	T2	20040122	JP 2002-505044	20010611
US 2003181359	A1	20030925	US 2002-311519	20021213
PRAI US 2000-212880P	P	20000614		
WO 2001-US40925	W	20010611		

OS CASREACT 136:86054; MARPAT 136:86054
AB The prodrug of the invention is a modified form of a therapeutic agent and comprises a therapeutic agent, an oligopeptide AA3-AA2-AA1 (AA1 is leucine, phenylalanine, isoleucine, alanine, glycine, tyrosine, 2-naphthylalanine, or serine; AA2 is alanine, leucine, tyrosine, glycine, serine, 3-pyridylalanine, 2-thienylalanine, aminoisobutyric acid, threonine, or phenylalanine; AA3 is leucine, sarcosine, tyrosine, phenylalanine, p-chloro- or p-nitrophenylalanine, valine, norleucine, norvaline, phenylglycine, tryptophan, tetrahydroisoquinoline-3-carboxylic acid, 3-pyridylalanine, alanine, glycine, 2-thienylalanine, methionine, or proline), a stabilizing group and, optionally, a linker group. The prodrug is cleavable by a trouase enzyme such as Thimet oligopeptidase.

L14 ANSWER 8 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Thus, Suc-Leu-Ala-Leu-Dox (Suc = succinic acid residue, Dox = doxorubicin
residue), prepd. by conjugation of doxorubicin hydrochloride with Fmoc-Leu-Ala-Leu-OH, deprotection, and acylation with succinic anhydride,
showed tumor-activated prodrug activity on LNCaP, HT-29 and PC-3 cells of
0.016, 0.052, and 0.075 μM, resp. Suc-Leu-Ala-Leu-Dox is better tolerated in vivo than is doxorubicin.
IT **154889-68-6**, KW 2189
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tripeptide prodrug compds.)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



L14 ANSWER 9 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:923644 CAPLUS
DN 136:58787
TI Enzyme-cleavable prodrug compounds
IN Nieder, Matthew H.; Dubois, Vincent; Gangwar, Sanjeev; Lobl, Thomas J.;
Pickford, Leslie B.; Trouet, Andre; Yarranton, Geoffrey T.
PA Corixa Corporation, USA
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

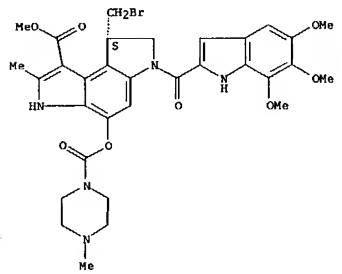
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095945	A2	20011220	WO 2001-US18903	20010611
	WO 2001095945	A3	20020815		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1294405	A2	20030326	EP 2001-950291	20010611
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004510703	T2	20040408	JP 2002-510122	20010611
PRAI	US 2000-211887P	P	20000614		
	US 2001-290448P	P	20010511		
	WO 2001-US18903	W	20010611		

OS MARPAT 136:58787
AB The prodrug of the invention is a modified form of a therapeutic agent and
comprises a therapeutic agent, an oligopeptide, a stabilizing group and,
optionally, a linker group. The prodrug is cleavable by the enzyme, thimet oligopeptidase (TOP). Also disclosed are methods of designing prodrugs by utilizing TOP-cleavage sequences within the conjugate and methods of treating patients with prodrugs of the invention.
IT **154889-68-6**, KW-2189
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enzyme-cleavable prodrug compds.)

L14 ANSWER 9 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



L14 ANSWER 10 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:923642 CAPLUS
DN 136:74618
TI Prodrug compounds with isoleucine
IN Pickford, Lesley B.; Gangwar, Sanjeev; Lobl, Thomas J.; Nieder, Matthew
H.; Yarranton, Geoffrey T.
PA Corixa Corporation, USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

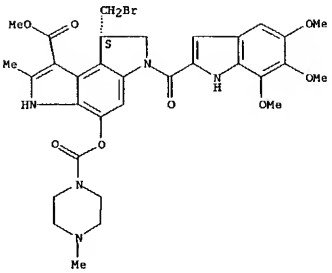
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095943	A2	20011220	WO 2001-US18857	20010611
	WO 2001095943	A3	20020829		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1294404	A2	20030326	EP 2001-944442	20010611
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004510702	T2	20040408	JP 2002-510120	20010611
	US 2004039160	A1	20040226	US 2002-311411	20021213
PRAI	US 2000-211686P	P	20000614		
	WO 2001-US18857	W	20010611		

OS MARPAT 136:74618
AB The compds. of the invention are modified forms of therapeutic agents. A
typical prodrug compound of the invention comprises a therapeutic agent, an
oligopeptide having an isoleucine residue, a stabilizing group and,
optionally, a linker group. The prodrug is cleavable by an enzyme associated
with the target cell. Methods of making and using the compds. are also
disclosed.
IT **154889-68-6**, Kw-2189
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prodrug compds. with isoleucine)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

L14 ANSWER 10 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 11 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:479762 CAPLUS
DN 135:81987
TI Sterilization of hardly water-soluble compounds by filtration
IN Kato, Hiromi; Tashiro, Yoshikazu
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

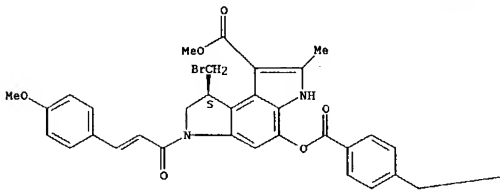
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001181207	A2	20010703	JP 1999-369550	19991227
PRAI JP 1999-369550		19991227		

OS MARPAT 135:81987
AB Hardly water-soluble pharmaceutically active agents, especially antitumor DC-89 derivs., are entrapped in liposomes having an average particle size of ≤ 0.2 μm and an injectable solution containing the liposomes is sterilizable by filtration.
IT **347174-93-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sterilization of hardly water-soluble compds. entrapped in liposomes by filtration)
RN 347174-93-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

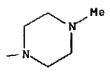
Absolute stereochemistry.
Double bond geometry unknown.

L14 ANSWER 11 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

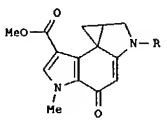


PAGE 1-B

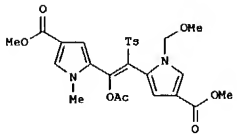


L14 ANSWER 12 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

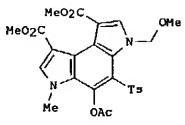
AN 2001:315840 CAPLUS
DN 135:76706
TI Derivatives of Methyl 5-Methyl-4-oxo-1,2,4,5,8,8a-hexahydrocyclopropa[c]-pyrrolo[3,2-e]indole-7- carboxylate: A Case of Inverse Electronic Effects on the Reactivity of CC-1065 Derivatives
AU Castedo, Luis; Delamano, Jose; Enjo, Juan; Fernandez, Jesus; Gravalos, Dolores G.; Leis, Ramon; Lopez, Carmen; Marcos, Carlos F.; Rios, Ana; Tojo, Gabriel
CS Departamento de Quimica Organica, Unidad Asociada al CSIC Universidad de Santiago de Compostela, Santiago de Compostela, 15706, Spain
SO Journal of the American Chemical Society (2001), 123(21), 5102-5103
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 135:76706
GI



I



II



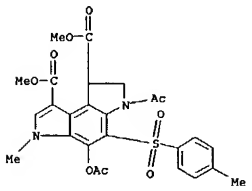
III

AB A series of Me 5-methyl-4-oxo-1,2,4,8,8a-hexahydrocyclopropa[c]-pyrrolo[3,2-e]indole-7-carboxylate derivs., I (R = H, CONH2, CO2C(Me)3, COMe, or SO2ME), were prepared A key reaction was the photochem. oxidative

L14 ANSWER 12 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
cyclization of bis-pyrrylethene II to produce intermediate III. These
novel 5-methyl-cyclopropaindolones were found to exhibit a non-linear solvolytic behavior, with a region of increased reactivity (log k) correlating with decreased electron-deficiency as reflected by the σp Hammett const. of their R substituents. Cyclopropaindolones I (R = H, CONH2, CO2C(Me)3, COMe, or SO2Me) also show an abnormal relationship
between solvolytic reactivity and in vitro cytotoxic potency relative to
other CC-1065 analogs, with those compds. with greater potency also having
greater solvolytic reactivity.

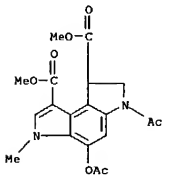
IT **170431-00-2P 170431-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(inverse electronic effects on the reactivity of 5-methyl-cyclopropaindolone CC-1065 derivs)

RN 170431-00-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-
1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl ester
(9CI) (CA INDEX NAME)



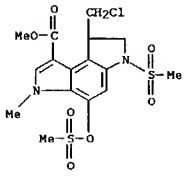
RN 170431-01-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-
1,2,3,6-tetrahydro-6-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 12 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **346669-65-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(inverse electronic effects on the reactivity of 5-methyl-cyclopropaindolone CC-1065 derivs)

RN 346669-65-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-
tetrahydro-3-methyl-6-(methylsulfonyl)-4-[(methylsulfonyl)oxy]-, methyl
ester (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:488720 CAPLUS
DN 133:266627
TI Synthesis and antitumor activity of duocarmycin derivatives: A-ring pyrrole compounds bearing β-(5',6',7'-trimethoxy-2'-indolyl)acryloyl group
AU Amishiro, N.; Nagamura, S.; Kobayashi, E.; Okamoto, A.; Gomi, K.; Okabe,
M.; Saito, H.
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Shizuoka, 411-8731, Japan
SO Bioorganic & Medicinal Chemistry (2000), 8(7), 1637-1643
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB A series of A-ring pyrrole derivs. of duocarmycin bearing the β-(5',6',7'-trimethoxy-2'-indolyl)acryloyl group were synthesized, and evaluated for in vitro anticellular activity against HeLa S3 cells and
in vivo antitumor activity against murine sarcoma 180 in mice. New Seg-B
analogs bearing the β-(5',6',7'-trimethoxy-2'-indolyl)acryloyl group containing a double bond as a spacer had lower peripheral blood toxicity than
the derivs. bearing the 5',6',7'-trimethoxyindole-2'-carboxyl group in
Seg-B of the natural type. Moreover, most of them exhibited potent antitumor activity against in vivo murine tumor models.

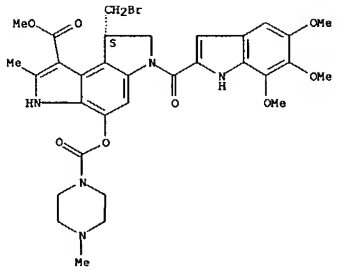
IT **154889-68-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(preparation and antitumor activity of duocarmycin derivs.)

RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **297137-23-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(preparation and antitumor activity of duocarmycin derivs.)

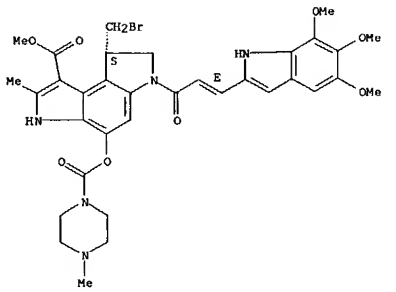
RN 297137-23-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(2E)-3-(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

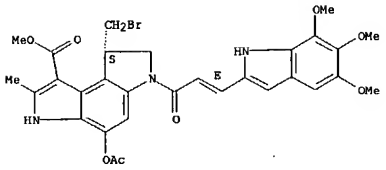
● HBr

IT **297137-24-7P 297137-25-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of duocarmycin derivs.)
RN 297137-24-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(2E)-3-(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

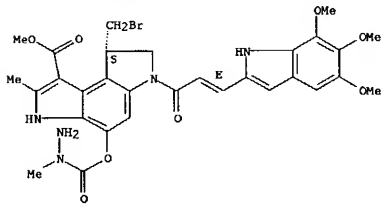
L14 ANSWER 13 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 297137-25-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-6-[(2E)-3-(5,6,7-trimethoxy-1H-indol-2-yl)-1-oxo-2-propenyl]-, methyl ester, (8S)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



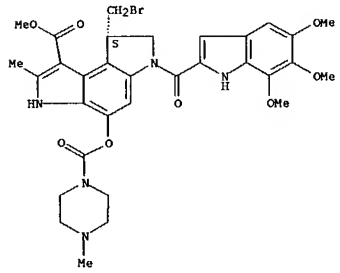
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:424475 CAPLUS
DN 133:26526
TI A phase II pilot study of KW-2189 in patients with advanced renal cell
carcinoma
AU Small, Eric J.; Figlin, Robert; Petrylak, Daniel; Vaughn, David J.; Sartor, Oliver; Horak, Ivan; Pincus, Rosemarie; Kremer, Alton; Bowden,
Chris
CS UCSF Comprehensive Cancer Center, University of California, San Francisco,
CA, USA
SO Investigational New Drugs (2000), 18(2), 193-197
CODEN: INNDDK; ISSN: 0167-6997
PB Kluwer Academic Publishers
DT Journal
LA English
AB KW-2189 is a semi-synthetic, water-soluble analog of duocarmycin B2, a new
class of potent antitumor antibiotics produced by streptomyces, with improved in vitro antitumor potency. Forty patients with pathol. confirmed metastatic renal cell carcinoma were treated in this multicenter, open-label phase II trial. All patients received 0.4 mg/m2
KW-2189 as an IV infusion for Cycle 1. Cycles were repeated every 5 to 6
wk with escalations to 0.5 mg/m2 in the absence of significant toxicity or
disease progression. No patient had an objective response. The most common drug-related toxicity was hematol.-delayed neutropenia and thrombocytopenia, with recovery by week 6. Non-hematol. toxicity consisted of mild to moderate fatigue, nausea and vomiting, and anorexia
that was generally manageable. KW-2189 in this dose and schedule has a
predictable safety profile of reversible myelosuppression. No activity in
metastatic renal cell carcinoma was demonstrated.
IT **154889-68-6**, KW-2189
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II pilot study of KW-2189 in patients with advanced renal cell
carcinoma)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 14 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

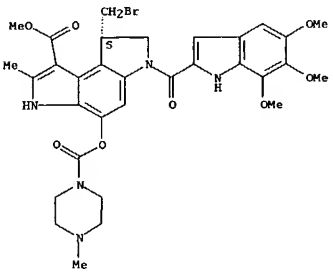
L14 ANSWER 15 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:401690 CAPLUS
DN 133:48878
TI Oligopeptide prodrug compounds and process for preparation thereof
IN Lobl, Thomas J.; Dubois, Vincent; Fernandez, Anne-Marie; Gangwar, Sanjeev;
Lewis, Evan; Nieder, Matthew H.; Trouet, Andre; Viski, Peter; Yarranton,
Geoffrey T.
PA Coulter Pharmaceutical, Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000033888	A2	20000615	WO 1999-US30393	19991210
	WO 2000033888	A3	20011108		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1144011	A2	20011017	EP 1999-967462	19991210
	EP 1144011	A3	20020206		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003518000	T2	20030603	JP 2000-586378	19991210
	AU 773420	B2	20040527	AU 2000-23733	19991210
	US 2002142955	A1	20021003	US 2001-879442	20010611
PRAI	US 1998-111793P	P	19981211		
	US 1999-119312P	P	19990208		
	WO 1999-US30393	W	19991210		
	US 2000-211887P	P	20000614		
	US 2001-290448P	P	20010511		

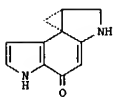
OS MARPAT 133:48878
AB The prodrug of the invention is a modified form of a therapeutic agent and
comprises a therapeutic agent, an oligopeptide, a stabilizing group and,

L14 ANSWER 15 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
optionally, a linker group. The prodrug is cleavable by the enzyme trouase. Also disclosed are processes for making the prodrug compds.
IT **154889-68-6**, KW-2189
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(oligopeptide prodrug compds. and process for preparation thereof)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



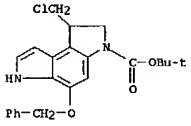
L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:301528 CAPLUS
DN 133:58647
TI Synthesis and Evaluation of 1,2,8,8a-Tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one, the Parent Alkylation Subunit of CC-1065 and the Duocarmycins: Impact of the Alkylation Subunit Substituents and Its Implications for DNA Alkylation Catalysis
AU Boger, Dale L.; Santillan, Alejandro, Jr.; Searcey, Mark; Brunette, Steven
R.; Wolkenberg, Scott E.; Hedrick, Michael P.; Jin, Qing
CS Department of Chemistry and The Skaggs Institute for Chemical Biology, The
Scripps Research Institute, La Jolla, CA, 92037, USA
SO Journal of Organic Chemistry (2000), 65(13), 4101-4111
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 133:58647
GI



I

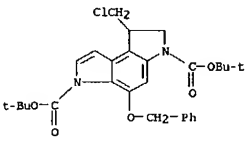
AB Synthesis of 1,2,8,8a-tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4(5H)-one
(I), the parent CC-1065 and duocarmycin SA alkylation subunit, is detailed. The parent CPI alkylation subunit lacks the C7 Me substituent
of the CC-1065 alkylation subunit and the C6 methoxycarbonyl group of duocarmycin SA, and their examination permitted the establishment of the impact
of these natural product substituents. The studies revealed a CPI stability comparable to the CC-1065 alkylation subunit but which was 6× more reactive than the (+)-duocarmycin SA alkylation subunit, and it displayed the inherent reaction regioselectivity (4:1) of the natural
products. The single-crystal X-ray structure of (+)-N-BOC-CPI depicts a
near identical stereoelectronic alignment of the cyclopropane accounting
for the identical reaction regioselectivity and a slightly diminished vinylogous amide conjugation relative to (+)-N-BOC-DSA suggesting that the
stability distinctions stem in part from this difference in the vinylogous
amide as well as alterations in the electronic nature of the fused pyrrole. Establishment of the DNA binding properties revealed that the

L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CPI-based agents retain the identical DNA alkylation selectivities of the
natural products. More importantly, the C6 methoxycarbonyl group of duocarmycin SA was found to increase the rate (12-13×) and efficiency (10×) of DNA alkylation despite its intrinsic lower reactivity while the CC-1065 C7 Me group was found to slow the DNA alkylation rate (4×) and lower the alkylation efficiency (ca. 4×). The greater DNA alkylation rate and efficiency for duocarmycin SA and related analogs contg. the C6 methoxycarbonyl is proposed to be derived from the extended length that the rigid C6 methoxycarbonyl provides and the resulting increase in the DNA binding-induced conformational change which serves to deconjugate the vinylogous amide and
activate the alkylation subunit for nucleophilic attack. The diminished
properties resulting from the CC-1065 C7 Me group may be attributed to the
steric impediment this substituent introduces to DNA minor groove binding
and alkylation. Consistent with this behavior, the duocarmycin SA C6 methoxycarbonyl group increases biol. potency while the CC-1065 C7 Me group diminishes it.
IT **227084-68-6P 277317-35-8P**
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and evaluation of tetrahydrocyclopropapyrroloindolones the
parent alkylation subunit of CC-1065 and the duocarmycins)
RN 227084-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



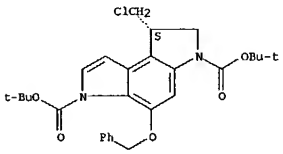
RN 277317-35-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-
dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX
NAME)

L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **277317-90-5P 277317-92-7P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and evaluation of tetrahydrocyclopropapyrroloindolones the
parent alkylation subunit of CC-1065 and the duocarmycins)
RN 277317-90-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-
dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester, (1S)- (9CI) (CA
INDEX NAME)

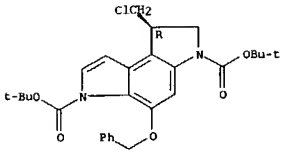
Absolute stereochemistry. Rotation (-).



RN 277317-92-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-3,6-dicarboxylic acid, 1-(chloromethyl)-1,2-
dihydro-5-(phenylmethoxy)-, bis(1,1-dimethylethyl) ester, (1R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 16 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



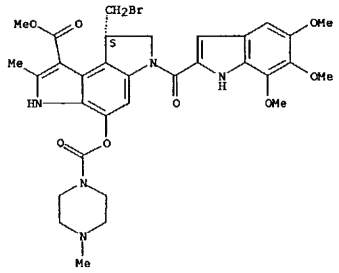
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:141730 CAPLUS
DN 132:334367
TI Synthesis and antitumor activity of duocarmycin derivatives: modification
at C-8 position of A-ring pyrrole compounds bearing the simplified
DNA-binding groups
AU Amishiro, N.; Nagamura, S.; Murakata, C.; Okamoto, A.; Kobayashi, E.; Asada, M.; Gomi, K.; Tamaoki, T.; Okabe, M.; Yamaguchi, N.; Yamaguchi, K.;
Saito, H.
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Nagaizumi, Sunto, Shizuoka, Japan
SO Bioorganic & Medicinal Chemistry (2000), 8(2), 381-391
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 132:334367
AB A series of the 8-O-substituted A-ring pyrrole derivs. of duocarmycin bearing the simplified DNA-binding moieties such as cinnamoyl or heteroaryl-acryloyl groups were synthesized, and evaluated for in vitro
anticellular activity against HeLa S3 cells and in vivo antitumor activity
against murine sarcoma 180 in mice. In addition, the stability of the
8-O-substituted analogs in aqueous solution and the conversion to their active
form (cyclopropane compound) from the 8-O-substituted analogs in mice or
human serum were examined The 8-O-substituted A-ring pyrrole derivs. bearing the simplified DNA-binding moieties showed remarkably potent in
vivo antitumor activity and low peripheral blood toxicity compared with
the 8-O-substituted A-ring pyrrole derivs. having the trimethoxyindole
skeleton in segment-B (Seg-B), which were equal to 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates and 4'-methoxy-β-heteroarylacrylates. Moreover, among 8-O-substituted analogs, several compds. can be chemical or enzymically converted to their
active form in human serum. This result indicated that new 8-O-substituted derivs. were different prodrugs from KW-2189 and 8-O-substituted analogs being the same type of prodrug as KW-2189.
IT **160819-28-3 186760-06-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(synthesis and antitumor activity of duocarmycin derivs. modified at
C-8 position of A-ring pyrrole compds. bearing the simplified DNA-binding groups)
RN 160819-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)-
(9CI) (CA INDEX NAME)

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

PAGE 1-A



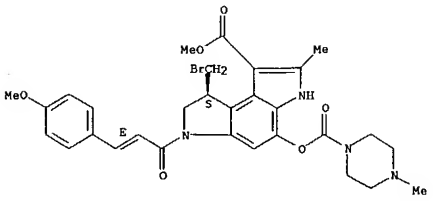
PAGE 2-A

● HBr

RN 186760-06-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

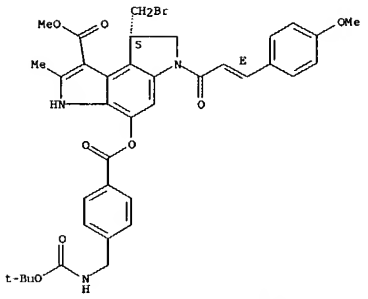


● HCl

IT 267899-52-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of duocarmycin derivs. modified at
C-8 position of A-ring pyrrole compds. bearing the simplified
DNA-binding groups)
RN 267899-52-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-
[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]benzoyl]oxy]-3,6,7,8-
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-,
methyl
ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

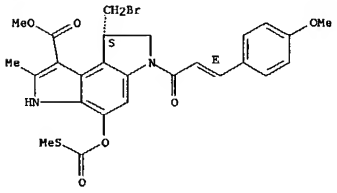
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 267899-40-1P 267899-41-2P 267899-42-3P
267899-43-4P 267899-44-5P 267899-45-6P
267899-46-7P 267899-47-8P 267899-48-9P
267899-49-0P 267899-50-3P 267899-51-4P
267899-53-6P 267899-54-7P 267899-55-8P
267899-56-9P 267899-57-0P 267899-58-1P
267899-59-2P 267899-60-5P 267899-61-6P
267899-62-7P 267899-64-9P 267899-65-0P
267899-66-1P 267899-67-2P 267899-68-3P
267899-69-4P 267899-70-7P 267899-71-8P
267899-72-9P 267899-73-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(synthesis and antitumor activity of duocarmycin derivs. modified at
C-8 position of A-ring pyrrole compds. bearing the simplified
DNA-binding groups)
RN 267899-40-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-
[[(methylthio)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

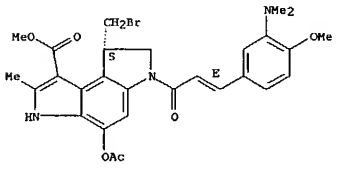
Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-41-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA
INDEX NAME)

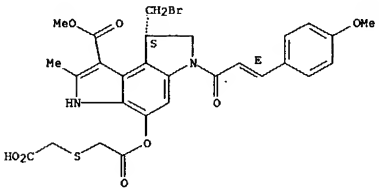
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-42-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

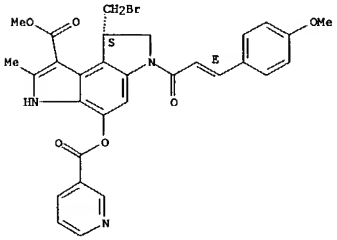
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-43-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

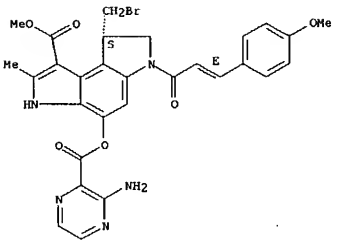


RN 267899-44-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[(3-

aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

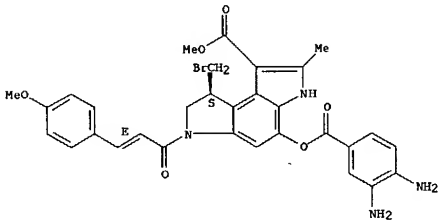


RN 267899-45-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[(3,4-

diaminobenzoyl)oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-

propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

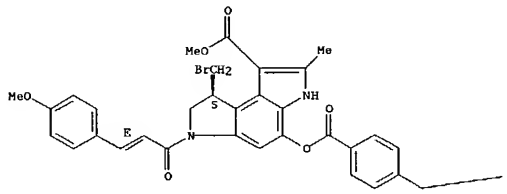


RN 267899-46-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[(4-aminobenzoyl)oxy]-8-

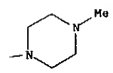
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



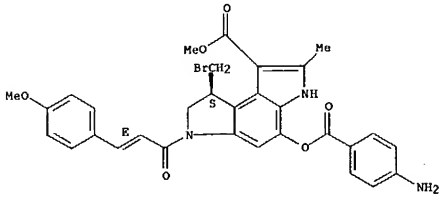
RN 267899-49-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-
4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,
(8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-
propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

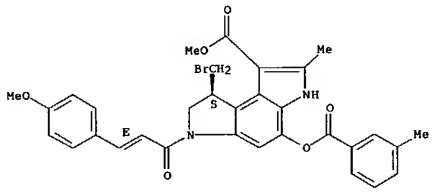
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-47-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-
methylbenzoyl)oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

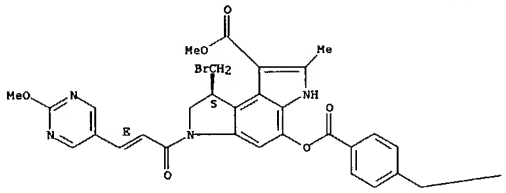


RN 267899-48-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

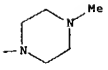
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

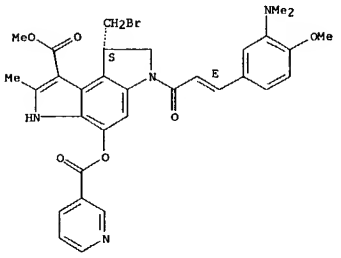


RN 267899-50-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

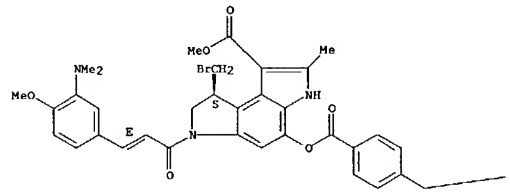


RN 267899-51-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

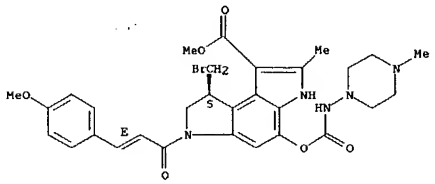
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

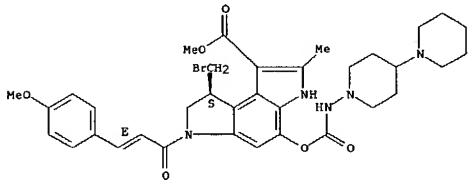
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-55-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[([1,4'-bipiperidin]-1'-

ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



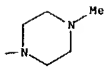
RN 267899-56-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

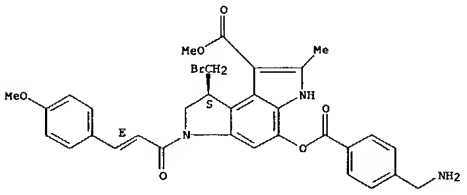
PAGE 1-B



RN 267899-53-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-

(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

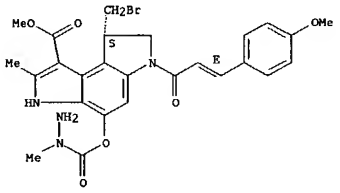
Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-54-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

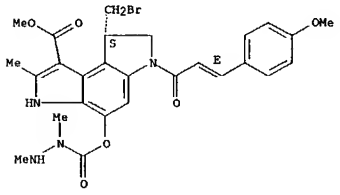
tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 267899-57-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

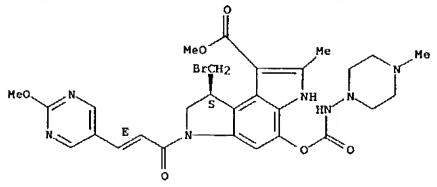


RN 267899-58-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

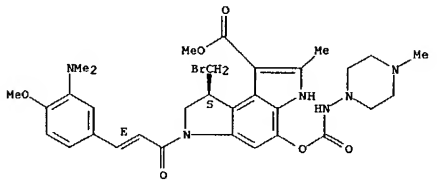
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 267899-59-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2
-
methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl
ester,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



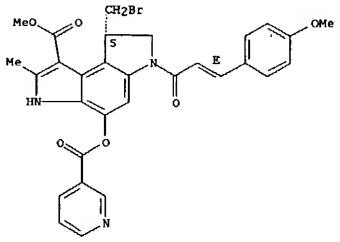
RN 267899-60-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2
-
methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (8S)-
(9CI)
(CA INDEX NAME)

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pyridinylcarbonyl)oxy]-, methyl ester, monohydrochloride, (8S)-
(9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

● HCl

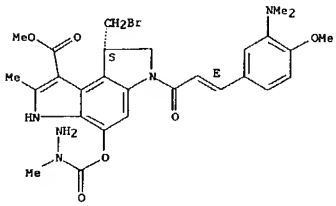
RN 267899-64-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

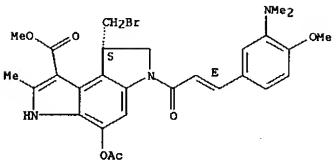
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.
Double bond geometry as shown.



RN 267899-61-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-
(bromomethyl)-6-[(2E)-3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-
propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester,
monohydrochloride,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



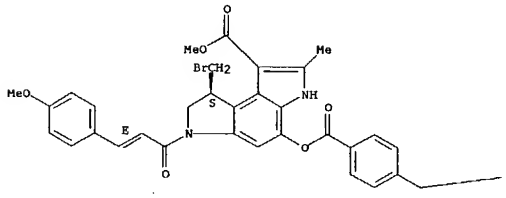
● HCl

RN 267899-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-

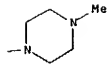
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



● HBr

PAGE 1-B



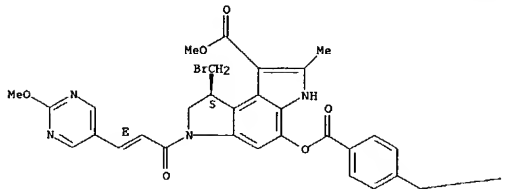
RN 267899-65-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-
4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,
dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

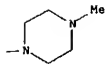
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



●2 HBr

PAGE 1-B

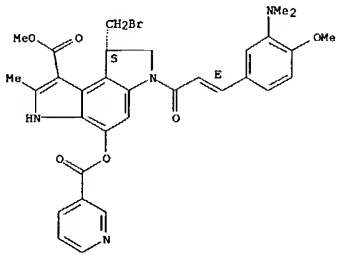


RN 267899-66-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2
-
methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, dihydrobromide,
(8S)-
(9CI) (CA INDEX NAME)

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

●2 HBr

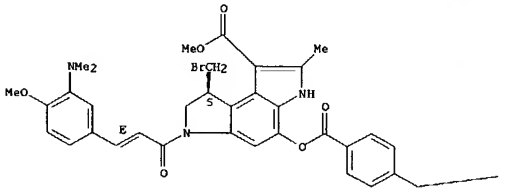
RN 267899-67-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[(2E)-3-

[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl
ester,
dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

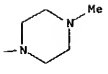
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



●2 HBr

PAGE 1-B

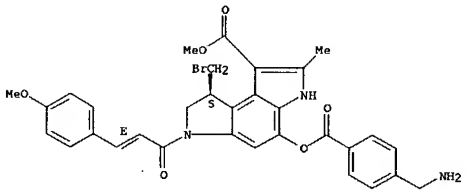


RN 267899-68-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-

(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester,
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

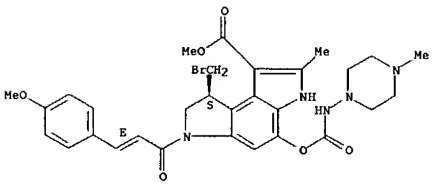


●HBr

RN 267899-69-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-
methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester,
dihydrobromide,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

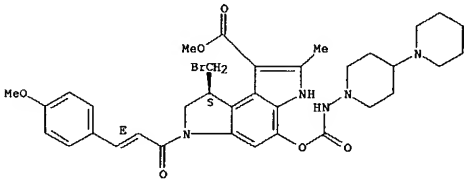


●2 HBr

RN 267899-70-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[([1,4'-bipiperidin]-1'-
ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-

L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, dihydrobromide,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



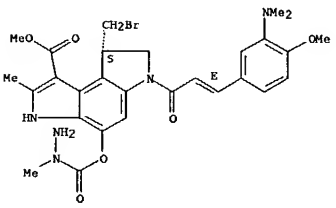
●2 HBr

RN 267899-71-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

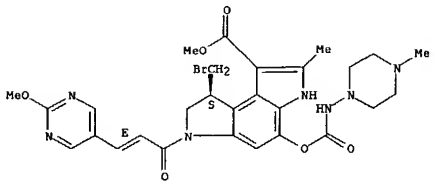
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-
[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, dihydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



●2 HBr

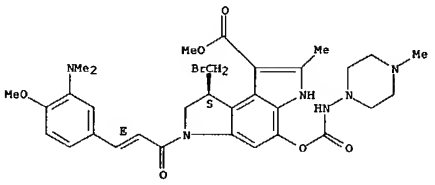
L14 ANSWER 17 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HBr

RN 267899-72-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[(2E)-3-
[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester,
monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

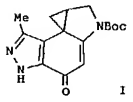
Absolute stereochemistry.
Double bond geometry as shown.



● HBr

RN 267899-73-0 CAPLUS

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:737584 CAPLUS
DN 132:78392
TI Resolution of a CPzI precursor, synthesis and biological evaluation of (+)
and (-)-N-Boc-CPzI: a further validation of the relationship between chemical solvolytic stability and cytotoxicity
AU Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto, Giampiero; Boyce, Christopher W.; Boger, Dale L.
CS Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara, 44100, Italy
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(21), 3087-3092
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI

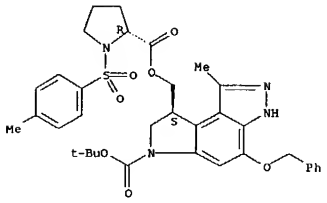


I

AB The chemical resolution, using N-tosyl-L-proline as a chiral auxiliary, of a
racemate of the pyrazole analog (±)-N-Boc-CPzI (I) of the left hand segment (CPI) of the antitumor agent CC-1065, and the cytotoxic evaluation
of both enantiomers are described. The reported results further validate
the direct relationship between chemical solvolytic stability of the cyclopropane ring and cytotoxicity proposed by Boger and coworkers.
IT **253598-42-4P 253598-46-8P**
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chemical resolution using N-tosyl-L-proline as a chiral auxiliary, solvolytic stability and cytotoxicity of CPzI moiety of CC-1065)
RN 253598-42-4 CAPLUS
CN D-Proline, 1-[(4-methylphenyl)sulfonyl]-, [(8S)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-1-methyl-4-(phenylmethoxy)pyrrolo[3,2-e]indazol-8-yl]methyl ester (9CI) (CA INDEX
NAME)

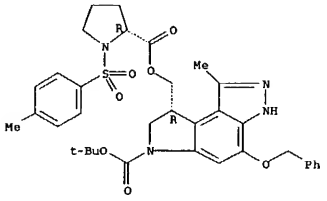
Absolute stereochemistry. Rotation (-).

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



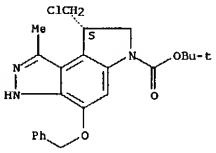
RN 253598-46-8 CAPLUS
CN D-Proline, 1-[(4-methylphenyl)sulfonyl]-, [(8R)-6-[(1,1-dimethylethoxy)carbonyl]-3,6,7,8-tetrahydro-1-methyl-4-(phenylmethoxy)pyrrolo[3,2-e]indazol-8-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



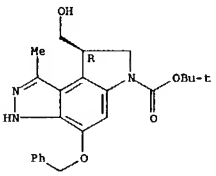
IT **187034-24-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(chemical resolution using N-tosyl-L-proline as a chiral auxiliary, solvolytic stability and cytotoxicity of CPzI moiety of CC-1065)
RN 187034-24-8 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



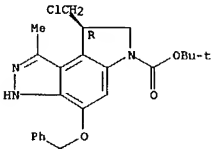
RN 253598-47-9 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

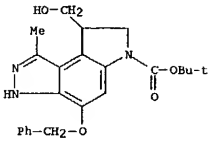


RN 253598-48-0 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

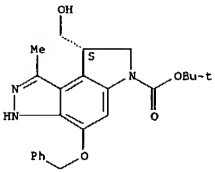


L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **253598-43-5P 253598-44-6P 253598-47-9P 253598-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chemical resolution using N-tosyl-L-proline as a chiral auxiliary, solvolytic stability and cytotoxicity of CPzI moiety of CC-1065)
RN 253598-43-5 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



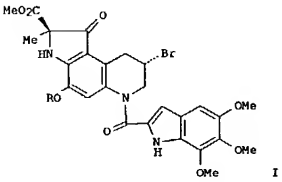
RN 253598-44-6 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 18 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:716681 CAPLUS
DN 132:49819
TI Synthesis and antitumor activity of water-soluble duocarmycin B1 prodrugs
AU Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Machida, 194-8533, Japan
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2995-2998
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I

AB The water-soluble duocarmycin B1 prodrugs such as I (R = β-D-glucopyranosyl; (OH)2OP; N-methylpiperazinylcarbonyl) were synthesized for improving biol. and pharmaceutical profiles of duocarmycin. Among these prodrugs, I (R = N-methylpiperazinylcarbonyl) exhibited potent antitumor activity against several human tumors in vivo.

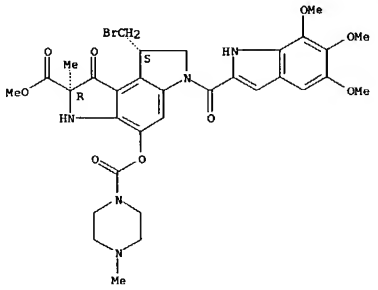
IT **171599-29-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of water-soluble duocarmycin B1 prodrugs)

RN 171599-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-

L14 ANSWER 19 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

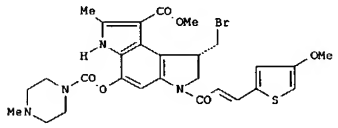


PAGE 2-A

● HCl

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:674932 CAPLUS
DN 132:22791
TI Synthesis and antitumor activity of duocarmycin derivatives: a-ring pyrrole compounds bearing 5-membered heteroarylacryloyl groups
AU Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Okamoto, Akihiko; Gomi, Katsushige; Saito, Hiromitsu
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company, Ltd., Shizuoka, 411-8731, Japan
SO Chemical & Pharmaceutical Bulletin (1999), 47(10), 1393-1403
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
OS CASREACT 132:22791
GI



I

AB A series of A-ring pyrrole compds. of duocarmycin bearing 5-membered heteroarylacryloyl groups (thienylacryloyl and pyrrolylacryloyl) and heteroarylcarbonyl groups were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. Most of the thienylacrylates displayed in vitro anticellular activity equivalent to 4'-methoxycinnamates. Among the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of methoxy-thienylacrylates, compound I, having 4'-methoxy-2'-thienylacryloyl as segment-B (Seg-B), showed remarkably potent antitumor activity and low peripheral blood toxicity in vivo, which were equal to those of 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates, compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B. On the other hand, the 2'-pyrrolylacrylates having a double bond as spacer showed 102- to 103-fold stronger anticellular activity than 2'-pyrrolecarboxylates (IC50<0.3 nM, 72h-exposure). The 8-O-acetate and 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 2'-pyrrolylacrylates exhibited an antitumor effect at a lower dose compared with the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. with a 4'-methoxycinnamoyl moiety. Moreover, it was expected that the antitumor activity would be increased by the strength of the extra hydrogen bond formed between the nitrogen of the pyrrole amido group and DNA, owing to the increase of the no. of N-methyl-2'-pyrrolecarboxamide units. However, 2'-pyrrolylacrylates having three N-methyl-2'-pyrrolecarboxamide units showed nearly equal antitumor activity to 2'-pyrrolylacrylates having only one N-methyl-2'-pyrrolecarboxamide unit.

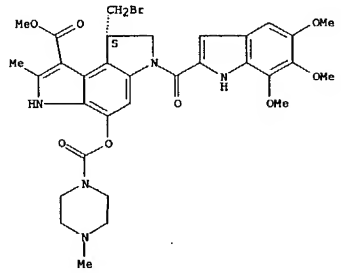
L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **160819-28-3 186760-06-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)

RN 160819-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

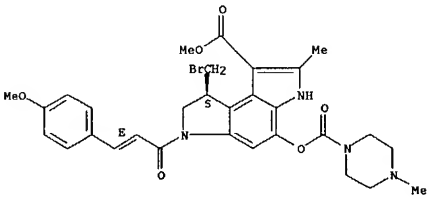
● HBr

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 186760-06-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



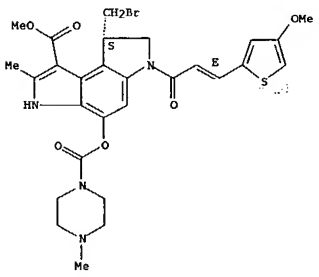
● HCl

IT **251999-64-1P 251999-94-7P 251999-95-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)
RN 251999-64-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(2E)-1-oxo-3-(2-thienyl)-2-propenyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

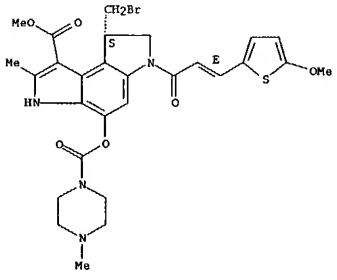
L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251999-95-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

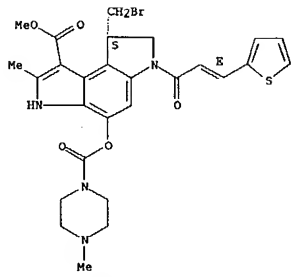
tetrahydro-6-[(2E)-3-(5-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **251999-68-5P 251999-73-2P 251999-74-3P**

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251999-94-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

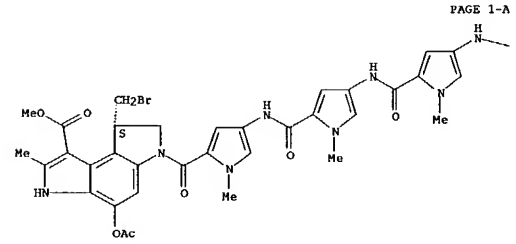
L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

251999-75-4P 251999-76-5P 251999-77-6P
251999-82-3P 251999-83-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of duocarmycin derivs. bearing 5-membered heteroarylacryloyl groups)
RN 251999-68-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-

yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



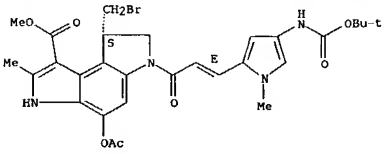
PAGE 1-B

RN 251999-73-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(bromomethyl)-6-[(2E)-3-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

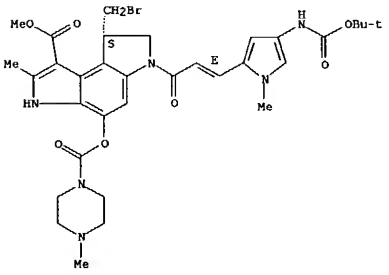
L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 251999-74-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[(2E)-3-

[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

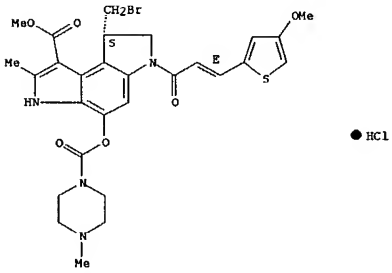
Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-75-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(2E)-1-oxo-3-(2-thienyl)-2-propenyl]-, methyl ester, monohydrochloride,
(8S)-

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

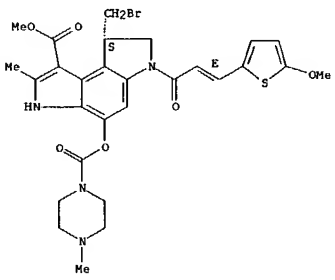


RN 251999-77-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(5-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride,
(8S)- (9CI) (CA INDEX NAME)

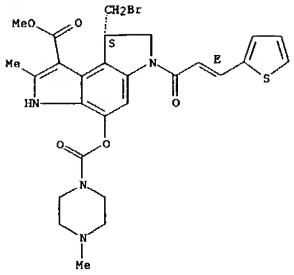
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 251999-76-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxy-2-thienyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

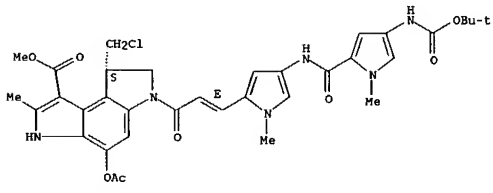
PAGE 2-A

RN 251999-82-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(chloromethyl)-6-[(2E)-3-[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-

methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



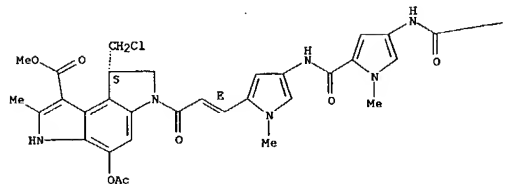
RN 251999-83-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(chloromethyl)-6-[(2E)-3-[4-[[[4-[[[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]carbonyl]amino]-1-methyl-1H-pyrrol-2-yl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

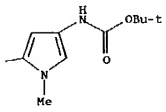
Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 20 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

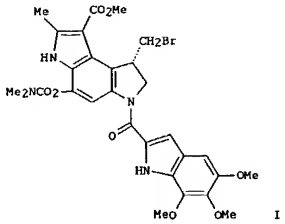


PAGE 1-B



RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:514023 CAPLUS
DN 131:322456
TI Antitumor antibiotics: duocarmycins
AU Nagamura, Satoru; Saito, Hiromitsu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Tokyo, 194, Japan
SO Chemistry of Heterocyclic Compounds (New York) (Translation of Khimiya Geterotsiklicheskikh Soedinenii) (1999), Volume Date 1998, 34(12), 1386-1405
CODEN: CHCCAL; ISSN: 0009-3122
PB Consultants Bureau
DT Journal
LA English
GI

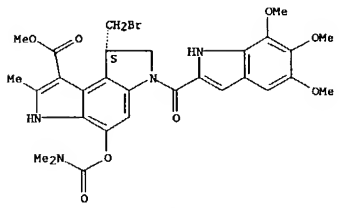


I

AB Duocarmycin A-ring pyrrole derivs. e.g. I, were prepared from duocarmycin B2
and B1 and were evaluated for antitumor activity. The IC50 of I against
HeLa S3 cells was 55 nM. The antitumor activity and relationship between
the phys. properties and biol. potency was studied.
IT **177958-20-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation and antitumor activity of duocarmycin derivs.)
RN 177958-20-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

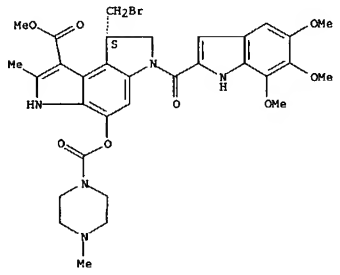


IT **154889-68-6P 160819-28-3P 177958-19-9P**
183240-24-6P 183240-25-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of duocarmycin derivs.)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

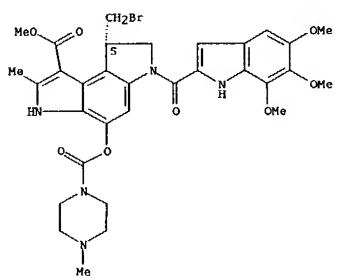


RN 160819-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

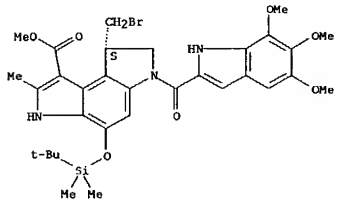
PAGE 2-A

● HBr

RN 177958-19-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

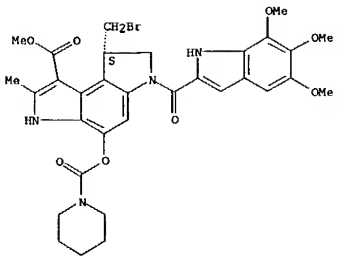


RN 183240-24-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

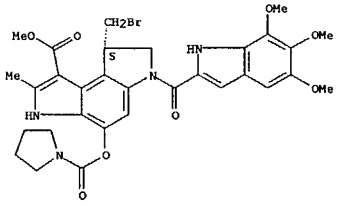
L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 183240-25-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

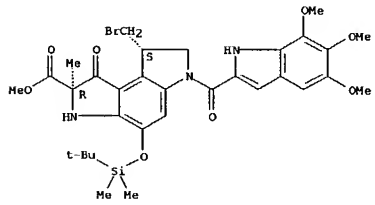


IT **129953-15-7P 129953-17-9P 183388-25-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and antitumor activity of duocarmycin derivs.)
RN 129953-15-7 CAPLUS

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-(9CI)
(CA INDEX NAME)

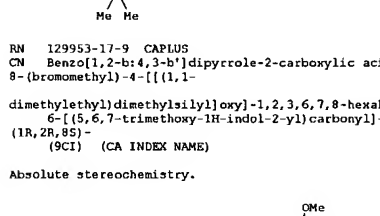
Absolute stereochemistry.



RN 129953-17-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

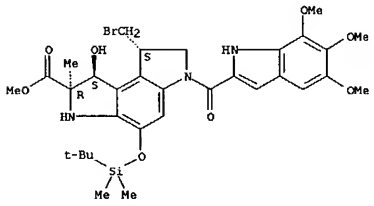


RN 183388-25-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2S,8S)-
(9CI) (CA INDEX NAME)

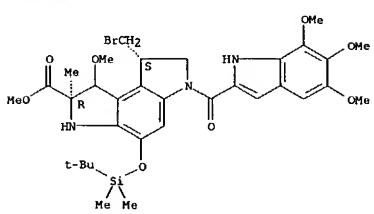
Absolute stereochemistry.



IT **248246-16-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antitumor activity of duocarmycin derivs.)
RN 248246-16-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-(9CI) (CA INDEX NAME)

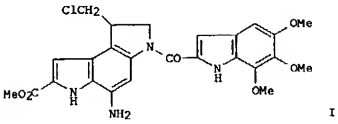
Absolute stereochemistry.



RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

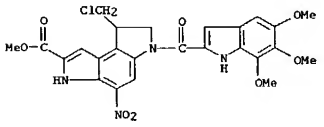
L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:439196 CAPLUS
DN 131:286298
TI Synthesis and Cytotoxicity of Amino-seco-DSA: An Amino Analogue of the DNA
Alkylating Agent Duocarmycin SA
AU Tercel, Moana; Gieseg, Michael A.; Denny, William A.; Wilson, William R.
CS Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of Auckland, Auckland, 92019, N. Z.
SO Journal of Organic Chemistry (1999), 64(16), 5946-5953
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 131:286298
GI



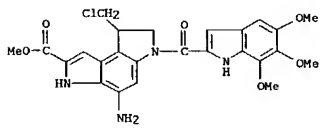
I

AB This paper describes the synthesis of Me 5-amino-1-(chloromethyl)-3-[(5,6,7-trimethoxyindol-2-yl)carbonyl]-1,2-dihydro-3H-pyrrolo[3,2-e]indole-7-carboxylate (I), an amino analog of the anticancer antibiotic and potent DNA minor groove alkylating agent seco-duocarmycin SA. Key points in the synthesis are sequential radical cyclization and Hemetsberger reaction steps to construct the indoline and indole rings of the target compound from a 1,2,3-trisubstituted benzene precursor. An intermediate has been resolved by chiral chromatog. to provide the sep. enantiomers of I. Racemic I alkylates DNA at adenine in AT rich sequences, similar to seco-duocarmycin SA and the previously reported amino-seco-CBI, but is 15-60 times less potent in an in vitro cytotoxicity test. Derivs. of I in which the amino group is replaced by an electron-withdrawing nitro or nitrobenzylcarbamate substituent are considerably less toxic and may have application as prodrugs to be activated selectively in a tumor environment.
IT **204915-56-0P 204915-57-1P 204915-59-3P**

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
204915-60-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxicity of amino-seco-DSA, prepn. of amino analog of DNA alkylating agent duocarmycin SA)
RN 204915-56-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

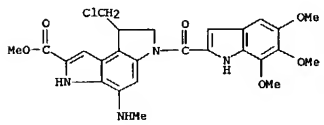


RN 204915-57-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

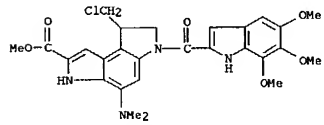


RN 204915-59-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-(methylamino)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

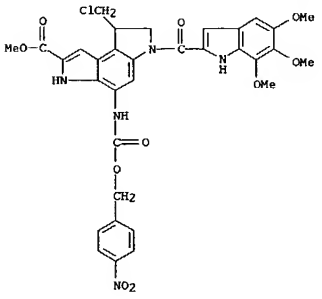


RN 204915-60-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-(dimethylamino)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



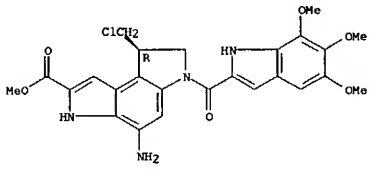
IT **204915-61-7P 246137-60-0P 246137-61-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog of DNA alkylating agent duocarmycin SA)
RN 204915-61-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-nitrophenyl)methoxy]carbonyl]amino]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



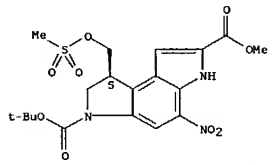
RN 246137-60-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



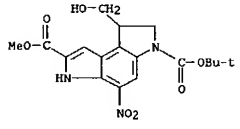
RN 246137-61-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **204916-10-9P 204916-11-0P 246137-52-0P 246137-56-4P 246137-57-5P 246137-58-6P 246137-59-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog of DNA alkylating agent duocarmycin SA)

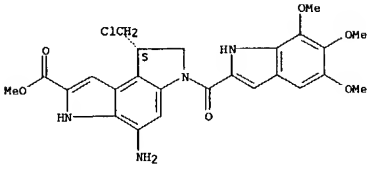
RN 204916-10-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 204916-11-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ester, (8S)- (9CI) (CA INDEX NAME)

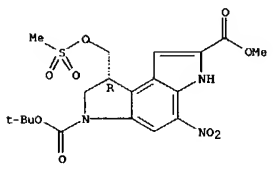
Absolute stereochemistry.



IT **246137-54-2P 246137-55-3P**
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog of DNA alkylating agent duocarmycin SA)

RN 246137-54-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8R)- (9CI) (CA INDEX NAME)

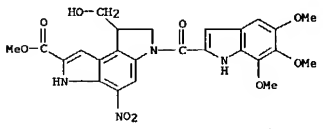
Absolute stereochemistry.



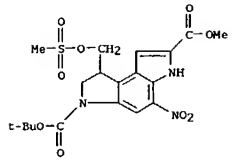
RN 246137-55-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

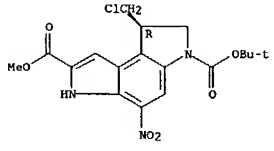


RN 246137-52-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-[[(methylsulfonyl)oxy]methyl]-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RN 246137-56-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8R)- (9CI) (CA INDEX NAME)

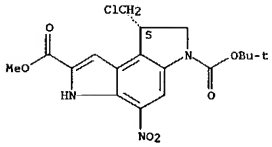
Absolute stereochemistry. Rotation (-).



RN 246137-57-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl ester, (8S)- (9CI) (CA INDEX NAME)

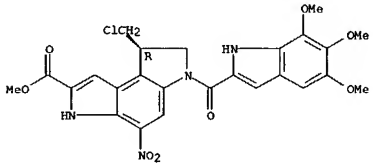
Absolute stereochemistry. Rotation (+).

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 246137-58-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8R)- (9CI) (CA INDEX NAME)

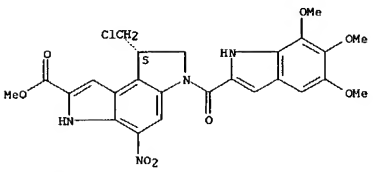
Absolute stereochemistry. Rotation (-).



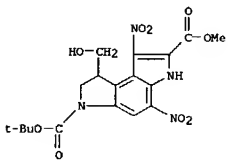
RN 246137-59-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 22 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

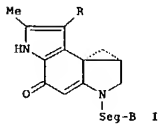


IT **246137-63-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and cytotoxicity of amino-seco-DSA, preparation of amino analog of DNA alkylating agent duocarmycin SA)
RN 246137-63-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1,4-dinitro-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:431081 CAPLUS
DN 131:286297
TI Synthesis and Antitumor Activity of Duocarmycin Derivatives: Modification of Segment-A of A-Ring Pyrrole Compounds
AU Amishiro, Nobuyoshi; Okamoto, Akihiko; Murakata, Chikara; Tamaoki, Tatsuya; Okabe, Masami; Saito, Hiromitsu
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company Ltd., Nagaizumi Sunto Shizuoka, 411-8731, Japan
SO Journal of Medicinal Chemistry (1999), 42(15), 2946-2960
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI

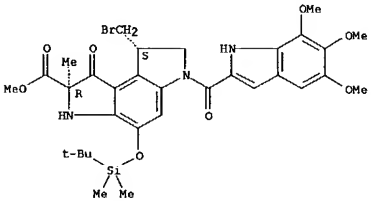


AB A series of 3-substituted A-ring pyrrole compds. of duocarmycin were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. These compds. were evaluated for peripheral blood toxicity and delayed lethal toxicity. Further, to expand the investigation of their peripheral blood toxicity, the toxicity to bone marrow cells (CFU-GM, CFU-Meg) was investigated. Among 3-substituted A-ring pyrrole compds. of duocarmycin bearing a 5',6',7'-trimethoxy-2'-indolecarboxyl (Q) group as segment-B, several analogs showed remarkably potent antitumor activity with low peripheral blood toxicity. The 3-formyl compound I [R = CHO, seg-B = Q] showed stronger antitumor activity with lower toxicity to bone marrow cells than DU-86, an active metabolite of KW-2189. However, this compound caused delayed death. On the other hand, the 3-bromo compound I [R = Br, seg-B = 4-methoxycinnamoyl] showed the most potent antitumor activity among the 4'-methoxycinnamate analogs with low toxicity to bone marrow cells. Furthermore, this compound did not cause delayed death. These results would indicate the importance of the C-3 substituents of A-ring pyrrole duocarmycin derivs. for exhibiting antitumor activity and decreasing toxicity.

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **129953-15-7 177958-19-9 246034-79-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor activity of duocarmycin derivs. with modified segment-A)
RN 129953-15-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

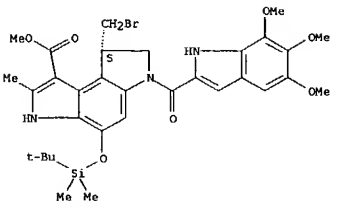
Absolute stereochemistry.



RN 177958-19-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

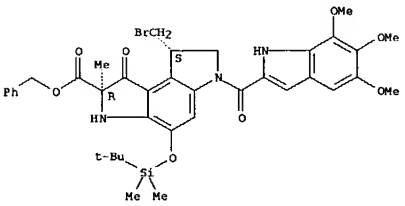
L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 246034-79-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester, (2R,8S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



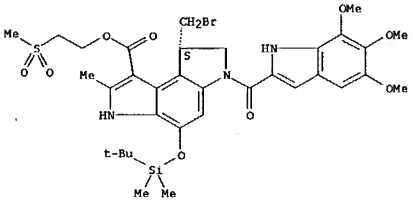
IT **205050-84-6P 205051-09-8P 205051-11-2P**
205051-57-6P 205051-58-7P 246034-75-3P
246034-76-4P 246034-77-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and antitumor activity of duocarmycin derivs. with modified
segment-A)

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 205051-11-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-(methylsulfonyl)ethyl ester, (8S)-
(9CI) (CA INDEX NAME)

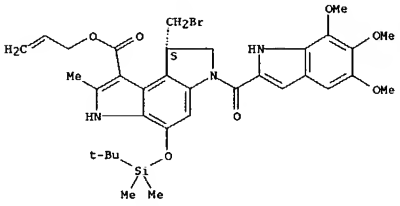
Absolute stereochemistry.



RN 205051-57-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

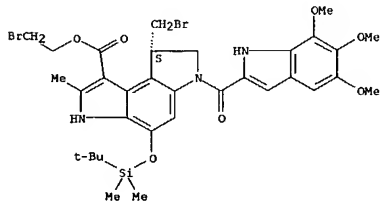


RN 205051-58-7 CAPLUS

L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 205050-84-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-bromoethyl ester, (8S)- (9CI) (CA
INDEX NAME)

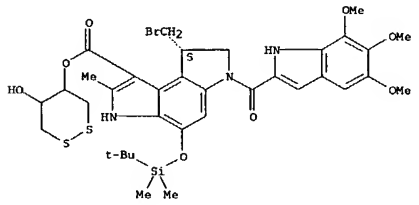
Absolute stereochemistry.



RN 205051-09-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 5-hydroxy-1,2-dithian-4-yl ester, (8S)- (9CI) (CA INDEX NAME)

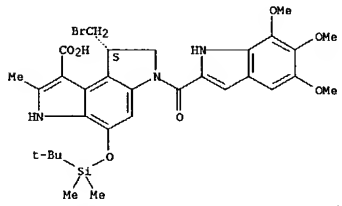
Absolute stereochemistry.



L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, (8S)- (9CI) (CA INDEX NAME)

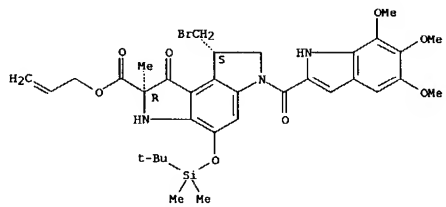
Absolute stereochemistry.



RN 246034-75-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

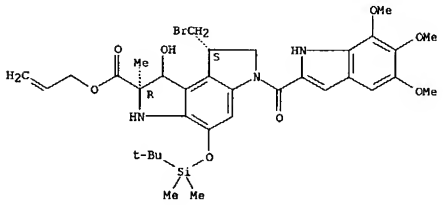


RN 246034-76-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-

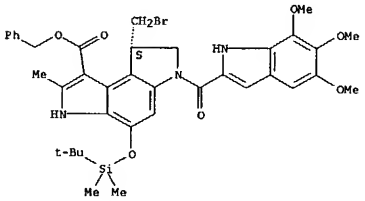
L14 ANSWER 23 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 246034-77-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



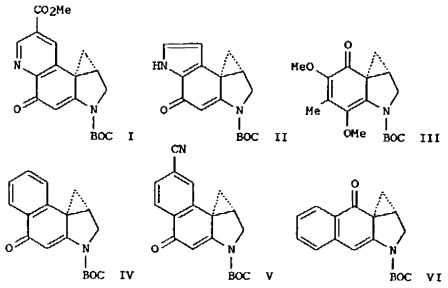
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 24 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:388148 CAPLUS
DN 131:44697
TI Synthesis of CC-1065/duocarmycin analogs
IN Boger, Dale L.
PA The Scripps Research Institute, USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

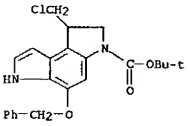
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9929642	A1	19990617	WO 1998-US25992	19981208
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2313231	AA	19990617	CA 1998-2313231	19981208
	AU 9918079	A1	19990628	AU 1999-18079	19981208
	EP 1037865	A1	20000927	EP 1998-962954	19981208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2001525382	T2	20011211	JP 2000-524241	19981208
	NZ 504884	A	20021025	NZ 1998-504884	19981208
	NO 2000002900	A	20000808	NO 2000-2900	20000607
	US 6310209	B1	20011030	US 2000-581049	20000710
	US 2002082424	A1	20020627	US 2001-1611	20011030
PRAI	US 1997-67960P	P	19971208		
	WO 1998-US25992	W	19981208		
	US 2000-581049	A3	20000710		

OS CASREACT 131:44697
GI

L14 ANSWER 24 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB The dihydroindole C-ring found in CC-1065/duocarmycin analogs is formed by the 5-exo-trig radical cyclization of an aryl halide onto a tethered vinyl chloride forming with chlorine installed as a suitable leaving group for subsequent cyclopropane spirocyclization. The versatility of this approach is disclosed in the context of six CC-1065/duocarmycin analogs (I-VI) previously synthesized in this laboratory
IT **227084-68-6P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the synthesis of CC-1065/duocarmycin analogs)
RN 227084-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 24 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

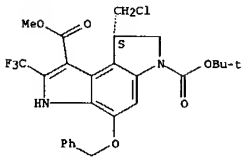
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:210305 CAPLUS
DN 130:338038
TI Novel cyclopropapyrroloindole derivative (AT-3510) bearing methoxycarbonyl
and trifluoromethyl groups
AU Fukuda, Yasumichi; Furuta, Hirosuke; Kusama, Yoshie; Ebisu, Hiroyuki; Oomori, Yasuo; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Company Ltd., Mitarai
Nogi Tochigi, 329-0114, Japan
SO Journal of Medicinal Chemistry (1999), 42(8), 1448-1458
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The seco-Cl 3-methoxycarbonyl-2-trifluoromethylcyclopropapyrroloindole (MCTFCPI) derivs. dl- and/or (S)-I [Ar = Q, Q1, Q2, Q3, R = 4,5,6-(MeO)3, 5,6,7-(MeO)3, 5-MeO, etc., X = NH, O, CH, Y = CH, N] carrying various acyl moieties at the N6-position were synthesized along with their prodrugs (S)-II, and their antitumor activity was evaluated. Among these derivs., AT-3510 [(S)-II (Ar = Q1, R = 7-MeO, X = O)], the novel prodrug MCTFCPI derivative carrying a 5-(7-methoxybenzofuran-2-ylcarbonyl)aminoindole-2-carbonyl group at the N6-position, was found to exhibit more excellent antitumor activity against human tumor xenografts than the clin. trial candidates carzelesin and KW-2189 (III) and cisplatin.
IT **157823-12-6P 157904-26-2P 157904-27-3P**
194093-62-4P 194093-63-5P 194093-64-6P
224321-50-0P 224321-51-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(intermediate in preparation, antitumor activity, and cytotoxicity of
pyrroloindole derivs.)
RN 157823-12-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

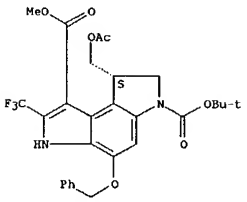
Absolute stereochemistry. Rotation (-).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157904-26-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

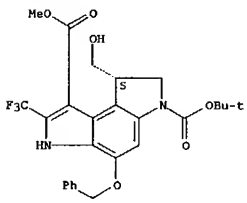
Absolute stereochemistry. Rotation (-).



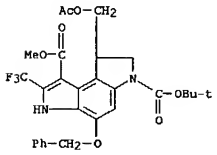
RN 157904-27-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

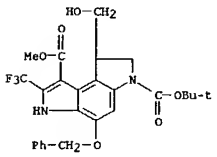
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



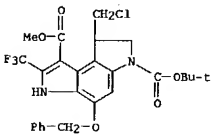
RN 194093-62-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-63-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 194093-64-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

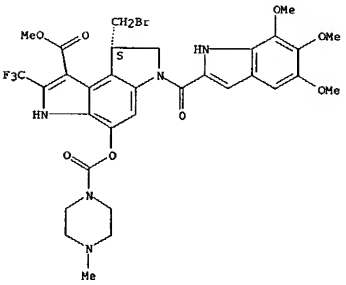


RN 224321-50-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI)
(CA INDEX NAME)

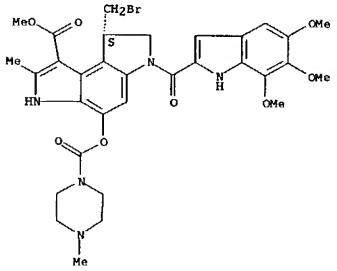
Absolute stereochemistry. Rotation (-).



L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.



IT **157823-41-1P 157823-42-2P 157823-43-3P**
157823-45-5P 157904-34-2P 194361-61-0P
224321-52-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, antitumor activity, and cytotoxicity of pyrroloindole derivs.)
RN 157823-41-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-

yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-

, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

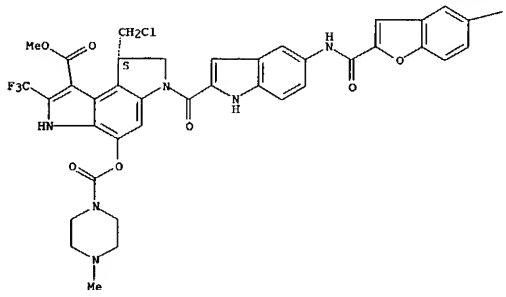
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 224321-51-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-

yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-
, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



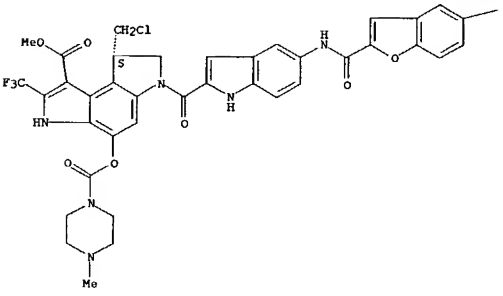
PAGE 1-B

—OMe

IT **154889-68-6**, KW-2189
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(preparation, antitumor activity, and cytotoxicity of pyrroloindole derivs.)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

—OMe

● HCl

RN 157823-42-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

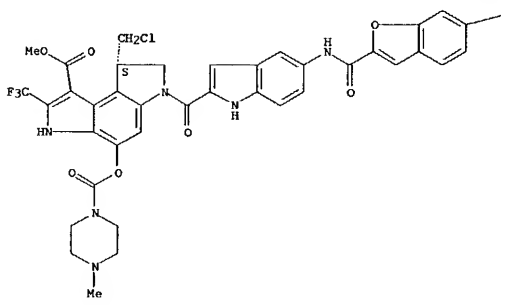
tetrahydro-6-[[5-[[(6-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-

yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-
, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

—OMe

● HCl

RN 157823-43-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)
-
6-[[5-[[(5,6,7-trimethoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-
yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
INDEX

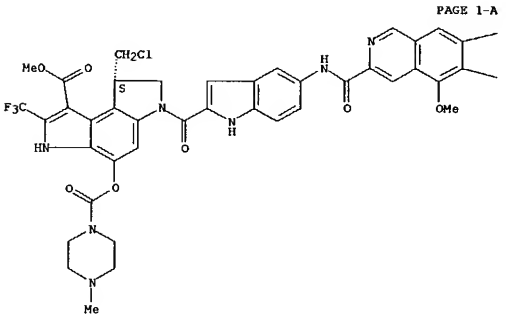
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 157823-45-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6
-
[[5-[[(5,6,7-trimethoxy-3-isoquinolinyl)carbonyl]amino]-1H-indol-2-
yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—OMe

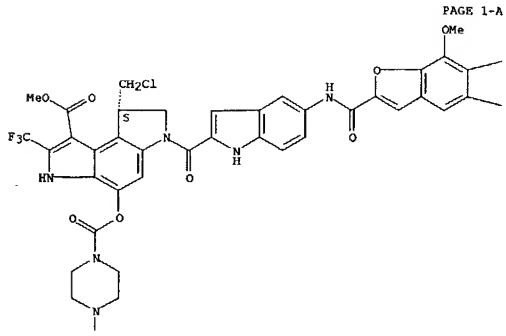
—OMe

● HCl

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

—OMe

—OMe

PAGE 2-A

● HCl

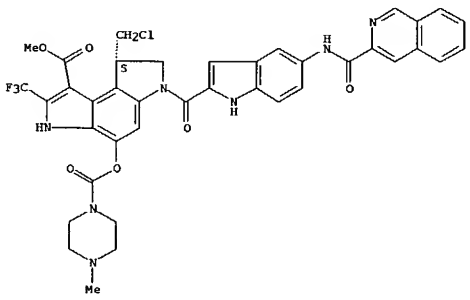
L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 157904-34-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl
ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

● HCl

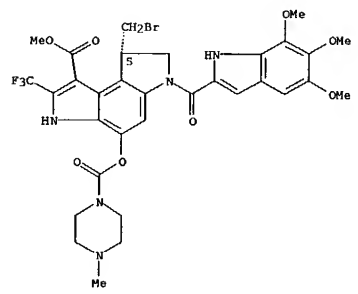
RN 194361-61-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

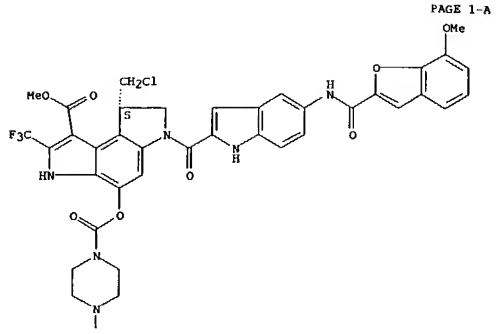
● HCl

RN 224321-52-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 25 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

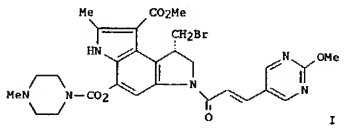


PAGE 2-A

● HCl

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:73220 CAPLUS
DN 130:252170
TI New Water-Soluble Duocarmycin Derivatives: Synthesis and Antitumor Activity of A-Ring Pyrrole Compounds Bearing β-Heteroarylacryloyl Groups
AU Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Pharmaceutical Research Institute, Kyowa Hakko Kogyo Company Ltd., Nagaizumi Sunto Shizuoka, 411-0943, Japan
SO Journal of Medicinal Chemistry (1999), 42(4), 669-676
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



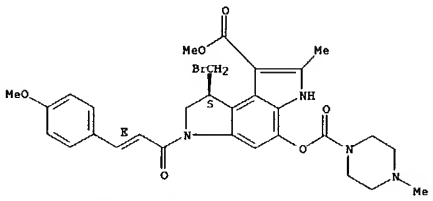
I

AB A series of A-ring pyrrole compds. of duocarmycin bearing 4'-methoxy-β-heteroarylacryloyl groups were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity against murine sarcoma 180 in mice. Most of the 4'-methoxy-β-heteroarylacrylates displayed in vitro anticellular activity equivalent to that of 4'-methoxycinnamates. Among the 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxy-β-heteroarylacrylates, compound I·HCl having a (4-methoxy-3,5-pyrimidinyl)acryloyl as segment-B (Seg-B) showed remarkably potent in vivo antitumor activity and low peripheral blood toxicity compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in Seg-B, which were equal to 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxycinnamates. Moreover, these 8-O-[(N-methylpiperazinyl)carbonyl] derivs. of 4'-methoxy-β-heteroarylacrylates had high aqueous solubility

IT **186760-19-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and antitumor activity of β-heteroarylacryloyl group bearing pyrrole analogs of duocarmycin)

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 186760-19-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

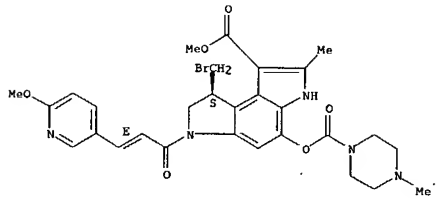
Absolute stereochemistry.
Double bond geometry as shown.



IT **221549-89-9P 221549-92-4P 221549-95-7P**
221549-99-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of β-heteroarylacryloyl group bearing pyrrole analogs of duocarmycin)
RN 221549-89-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

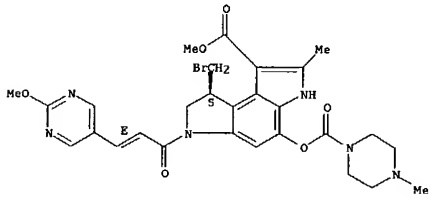


● HCl

RN 221549-92-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

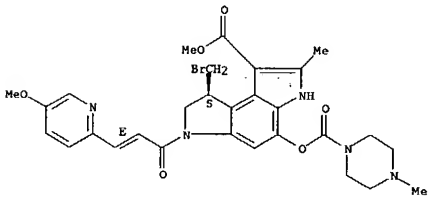
tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● HCl

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

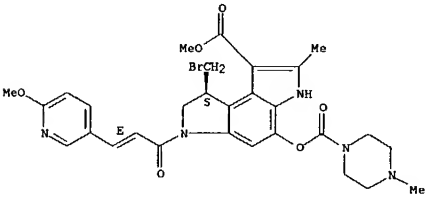


● HCl

IT **221549-88-8P 221549-91-3P 221549-94-6P**
221549-98-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(synthesis and antitumor activity of β-heteroarylacryloyl group
bearing pyrrole analogs of duocarmycin)
RN 221549-88-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-
[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

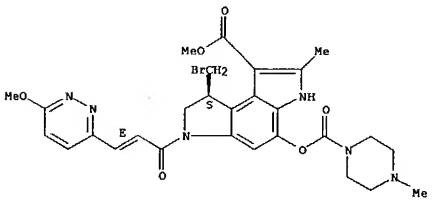
Absolute stereochemistry.
Double bond geometry as shown.



L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 221549-95-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● HCl

RN 221549-99-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

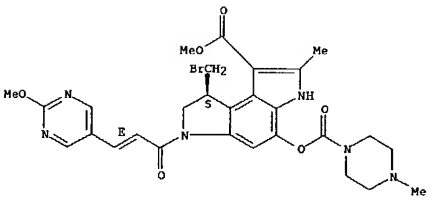
tetrahydro-6-[(2E)-3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-
[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride,
(8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 221549-91-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

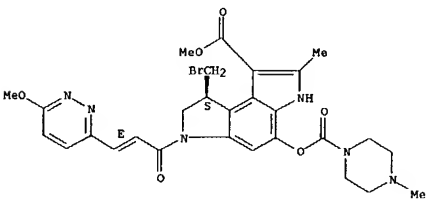
Absolute stereochemistry.
Double bond geometry as shown.



RN 221549-94-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI)
(CA
INDEX NAME)

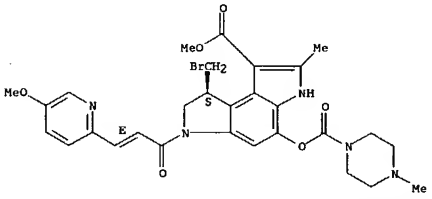
Absolute stereochemistry.
Double bond geometry as shown.



L14 ANSWER 26 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 221549-98-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

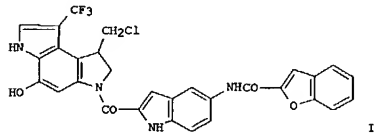
tetrahydro-6-[(2E)-3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

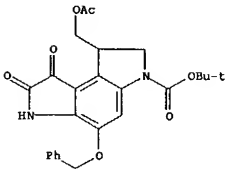
L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:32649 CAPLUS
DN 130:168271
TI Synthesis and cytotoxicity of various structural types of novel cyclopropapyrroloindole (CPI) derivatives
AU Fukuda, Yasumichi; Furuta, Hirosuke; Kusama, Yoshie; Ebisu, Hiroyuki; Oomori, Yasuo; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd, Nogi, Tochigi, 329-0114, Japan
SO Heterocycles (1998), 49, 53-58
CODEN: HTCYAM; ISSN: 0385-5414
PB Japan Institute of Heterocyclic Chemistry
DT Journal
LA English
GI



I

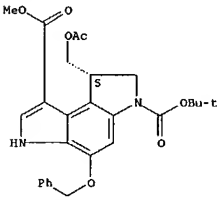
AB Various structural types of novel cyclopropapyrroloindole (CPI) derivs., e.g. I, were synthesized and their cytotoxicity was evaluated.
IT **132628-62-7 176685-39-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and antitumor activity of cyclopropapyrroloindole derivs.)
RN 132628-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



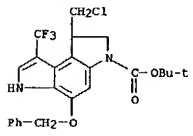
RN 176685-39-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



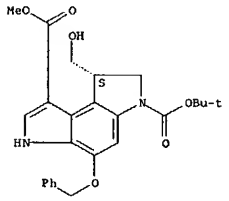
IT **176539-80-3P 176685-40-8P 176685-41-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of cyclopropapyrroloindole derivs.)
RN 176539-80-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-5-(phenylmethoxy)-8-(trifluoromethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



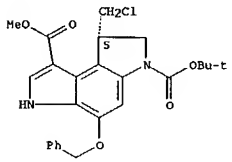
RN 176685-40-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 176685-41-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



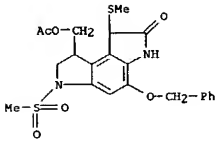
L14 ANSWER 27 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:721711 CAPLUS
DN 130:4029
TI Triplex forming oligonucleotides including pyrazolo(3,4-d)pyrimidine bases
IN Meyer, Rich B.; Gall, Alexander; Kutyavin, Igor V.
PA Epoch Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

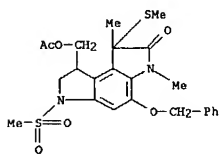
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9849180	A1	19981105	WO 1998-US8373	19980429
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, GH, GM, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6143877	A	20001107	US 1997-848373	19970430
AU 9872586	A1	19981124	AU 1998-72586	19980429
PRAI US 1997-848373	A	19970430		
WO 1998-US8373	W	19980429		

AB A triplex forming oligonucleotide is complementary pursuant to the G/T or
A/G recognition motif to a homopurine, or substantially homopurine target
sequence in double stranded nucleic acids, and at least one and preferably
all of the guanine bases are replaced by their pyrazolo[3,4-d]pyrimidine
analog, namely by 6-amino-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one. The
oligodeoxyribonucleotides containing the pyrazolo[3,4-d]pyrimidine analog of
guanine exhibit a lesser degree of self-association, and lack the nucleophilic
nitrogen atom in the 7 position of guanine. The latter feature results in
a diminished extent of self-crosslinking in ODNs which also have a
covalently attached crosslinking agent.
IT 112089-53-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(triplex forming oligodeoxyribonucleotides including pyrazolopyrimidine

L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
bases)
RN 112089-53-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



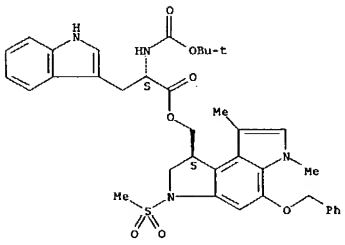
IT 192657-40-2P 192657-42-4P 192657-43-5P
215595-79-2P 215595-80-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(triplex forming oligodeoxyribonucleotides including pyrazolopyrimidine
bases)
RN 192657-40-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-1,3-dimethyl-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 192657-42-4 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [(1S)-1,2,3,6-tetrahydro-6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

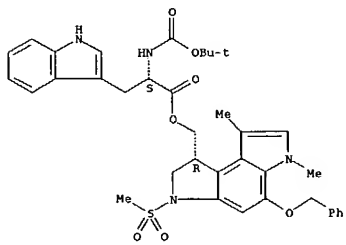
Absolute stereochemistry.

L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192657-43-5 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [(1R)-1,2,3,6-tetrahydro-6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

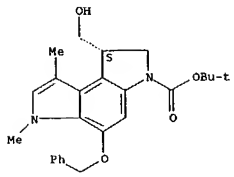
Absolute stereochemistry.



RN 215595-79-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-6,8-dimethyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (1S)- (9CI) (CA INDEX NAME)

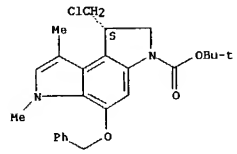
Absolute stereochemistry.

L14 ANSWER 28 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 215595-80-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-6,8-dimethyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

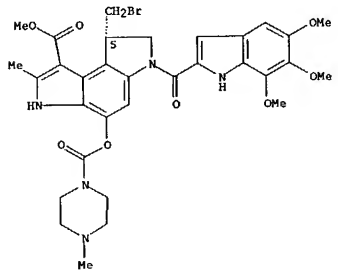


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 29 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:674015 CAPLUS
DN 130:75837
TI Phase I study of the duocarmycin semisynthetic derivative KW-2189 given daily for five days every six weeks
AU Alberts, Steven R.; Erlichman, Charles; Reid, Joel M.; Sloan, Jeff A.; Ames, Matthew M.; Richardson, Ronald L.; Goldberg, Richard M.
CS Divisions of Medical Oncology, Mayo Clinic, Rochester, MN, 55905, USA
SO Clinical Cancer Research (1998), 4(9), 2111-2117
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB The duocarmycins represent a new group of antitumor antibiotics produced by Streptomyces that bind to the minor groove of DNA. KW-2189 is a water-soluble semisynthetic derivative of duocarmycin B2, with significant activity in murine and human tumor models. We conducted a Phase I trial of KW-2189 in patients who had solid tumors that were refractory to standard chemotherapy or for whom no more effective therapy existed. KW-2189 was administered as a rapid i.v. bolus daily for 5 days every 6 wk. Twenty-two patients were enrolled and received a total of 31 cycles of KW-2189. Leukopenia, neutropenia, and thrombocytopenia were the dose-limiting toxicities, with nadirs occurring at medians of 36, 38, and 29 days, resp., at the 0.04 mg/m2/day dose level. Nonhematol. toxicities were mild, although one patient developed grade 3 fatigue. Four patients had stable disease over two to four cycles of treatment and showed no cumulative toxicity. The mean t1/2, plasma clearance, and steady-state volume of distribution were 13.5 min, 1,287 mL/min/m2, and 10,638 mL/m2, resp. Pharmacokinetics were similar on days 1 and 5, with no drug accumulation in plasma. The active metabolite DU-86 was not consistently found in patient plasma. For Phase II trials, when the 5 days every 6 wk schedule was used, 0.04 mg/m2/day KW-2189 appears to be the maximal tolerated dose, especially for patients who have received prior chemotherapy. At this dose level, the drug was well tolerated, and the toxicities were acceptable.
IT **154889-68-6**, KW-2189
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

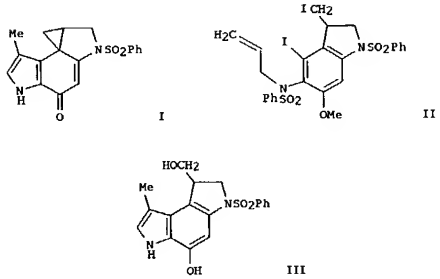
L14 ANSWER 29 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC
(Process); USES (Uses)
(duocarmycin semisynthetic deriv. KW-2189 toxicity and efficacy against chemotherapy-refractory solid tumors in humans)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



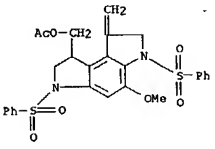
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 30 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:553501 CAPLUS
DN 129:289966
TI Efficient synthesis of the pharmacophore of the highly potent antitumor antibiotic CC-1065
AU Tietze, Lutz F.; Buhr, Wilm; Looft, Jan; Grote, Thomas
CS Institut fur Organische Chemie der Georg August-Universitat Gottingen, Gottingen, D-37077, Germany
SO Chemistry--A European Journal (1998), 4(8), 1554-1560
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
GI

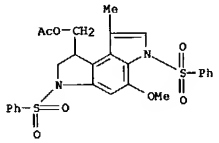


AB The pharmacophore CPI I of the potent antitumor antibiotic CC-1065 was synthesized in a very short reaction sequence of 11 steps with an overall yield of 23%. The key steps are two consecutive cyclizations mediated by organotransition metal complexes, which form first the pyrroline and then the pyrrole ring in I. Thus, halogen metal exchange of the N,N'-bisallylbromobenzene with Me3CLi and subsequent reaction with Cp2ZrMeCl gave II as a single product in 60% yield after quenching with two equivalent of iodine. Transformation of the iodomethyl group in II into an acetoxymethyl group, followed by Heck reaction, isomerization, and reductive cleavage, provided the pyrroloindoline system III, which was

L14 ANSWER 30 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
converted into I.
IT **165817-13-0P 165817-15-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(efficient synthesis of pharmacophore of highly potent antitumor antibiotic CC-1065)
RN 165817-13-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 1,2,3,6,7,8-hexahydro-5-methoxy-8-methylene-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)

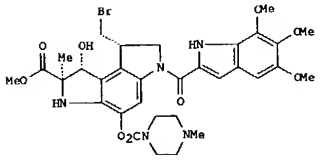


RN 165817-15-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 1,2,3,6-tetrahydro-5-methoxy-8-methyl-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

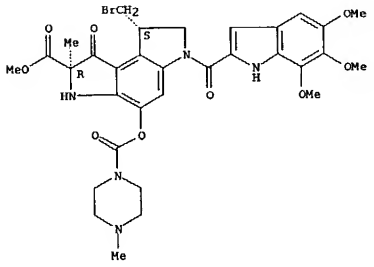
L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:536379 CAPLUS
DN 129:302469
TI Practical Synthesis of the High-Quality Antitumor Agent KW-2189 from Duocarmycin B2 Using a Facile One-Pot Synthesis of an Intermediate
AU Kinugawa, Masahiko; Nagamura, Satoru; Sakaguchi, Akihiko; Masuda, Yoshiaki; Saito, Hiromitsu; Ogasa, Takehiro; Kasai, Masaji
CS Sakai Research Laboratories, Kyowa Hakko Kogyo Co., Osaka, 590, Japan
SO Organic Process Research & Development (1998), 2(6), 344-350
CODEN: OPRDFK; ISSN: 1083-6160
PB American Chemical Society
DT Journal
LA English
GI



I

AB A facile and large-scale preparation process of a potent antitumor agent KW-2189, derived from the antitumor antibiotic duocarmycin B2, has been developed. This new synthetic route required three steps: (i) one-pot carbamoylation and subsequent reduction, (ii) Wagner-Meerwein rearrangement of the methoxycarbonyl group for the production of the pyrrole compound, and (iii) formation of the hydrobromide salt. The key strategic improvement was to obtain good quality hydroxy compound I in a reasonable yield without isolation of the unstable keto intermediate. During com.-scale production at a scale of about 50 g, this strategy provided high-quality KW-2189 in a 55% overall yield from duocarmycin B2. Potential degradation compds. were also synthesized and shown to be absent in the KW-2189 prepared
IT **154901-65-2P 160819-29-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(practical synthesis of high-quality antitumor agent KW-2189 from duocarmycin B2 using a facile one-pot synthesis of intermediate)
RN 154901-65-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

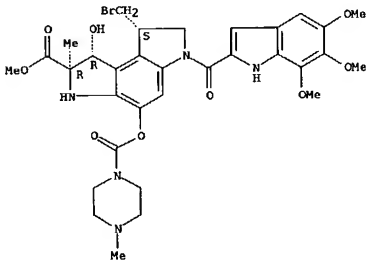
Absolute stereochemistry.



RN 160819-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

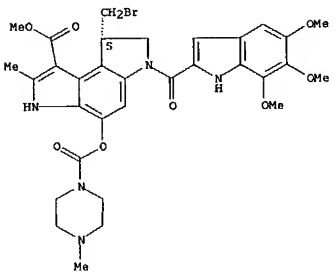
L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **154889-68-6P 160819-28-3P 171599-29-4P 214051-54-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(practical synthesis of high-quality antitumor agent KW-2189 from duocarmycin B2 using a facile one-pot synthesis of intermediate)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

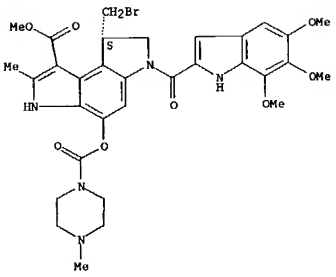


RN 160819-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

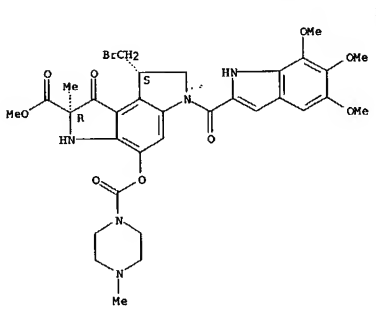
● HBr

RN 171599-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



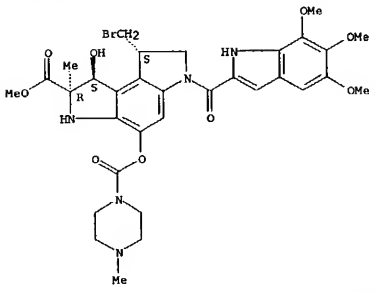
PAGE 2-A

● HCl

RN 214051-54-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1S,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 31 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:527333 CAPLUS
DN 129:161451
TI Preparation of antitumor and antimicrobial pyrroloindole derivatives and
their intermediates.
IN Fukuda, Yasumichi; Shimazawa, Rumiko; Oomori, Yasuo; Terashima, Shiro
PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832757	A1	19980730	WO 1998-JP234	19980122
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	JP 10265473	A2	19981006	JP 1998-7211	19980119
	AU 9855760	A1	19980818	AU 1998-55760	19980122
	EP 972775	A1	20000119	EP 1998-900695	19980122
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	TW 491846	B	20020621	TW 1998-87101164	19980123
	US 6080859	A	20000627	US 1999-341872	19990719
PRAI	JP 1997-11289	A	19970124		
	JP 1998-7211	A	19980119		
	WO 1998-JP234	W	19980122		

OS MARPAT 129:161451
GI

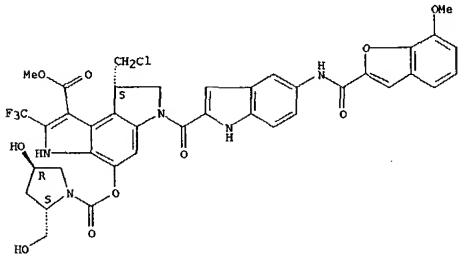
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = OH, pyrrolidinyl; n = 1, 2; R2 = lower (C1-4) alkyl; Y-Y or Y-X = CH2, CHOH, CH2-CH2, O-CH2 or NMe-CH2; Z1 = Cl or Br; and Ar1 = Q-Q4; Z2, Z3 = O, NH; m = 1-4 integer; and Ar2 = Q-Q3 *above*] *are* prepared Thus, II [R = H] was reacted with (2S)-pyrrolidine-2-methanol in

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 211053-33-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(2S,4R)-4-hydroxy-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, *methyl ester, (8S)-* (9CI) *(CA INDEX NAME)*

Absolute stereochemistry.

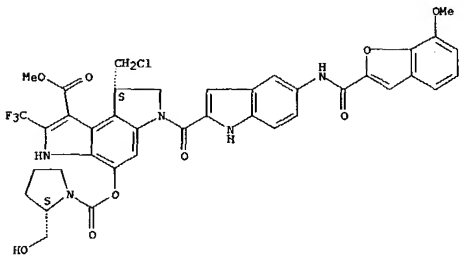


RN 211053-34-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[[(2S)-2-(1-pyrrolidinylmethyl)-1-pyrrolidinyl]carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

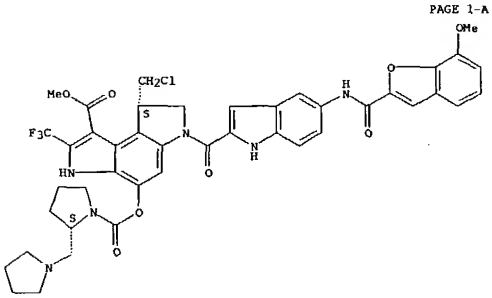
L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
THF contg. 4-nitrophenyl chloroformate and Et3N to give II [R = (S)-2-(hydroxymethyl)pyrrolidin-1-ylcarbonyl]. In an in vitro study using female mice II [R = 2-(hydroxymethyl)piperidinocarbonyl] (also prepd.) at 1.0 *mg/Kg s.c. showed ca.* 99% inhibition of the growth of adriamycin-resistant strain of M5076 cells. The stability of I was also studied.
IT **211053-32-6P 211053-33-7P 211053-34-8P**
211053-35-9P 211053-36-0P 211053-37-1P
211053-38-2P 211053-39-3P 211053-40-6P
211053-41-7P 211053-42-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor and antimicrobial pyrroloindole deriva. and their intermediates)
RN 211053-32-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(2S)-2-(hydroxymethyl)-1-pyrrolidinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



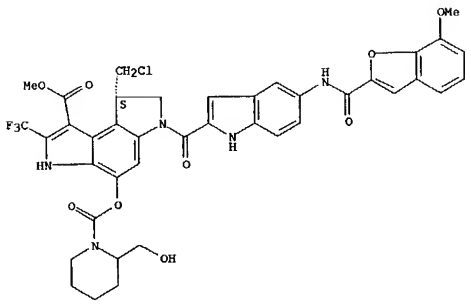
PAGE 2-A

● HCl

RN 211053-35-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[2-(hydroxymethyl)-1-piperidinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

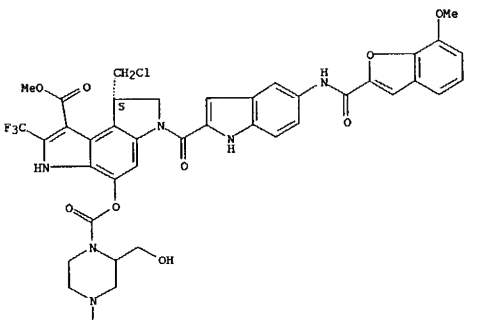


RN 211053-36-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[2-(hydroxymethyl)-4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

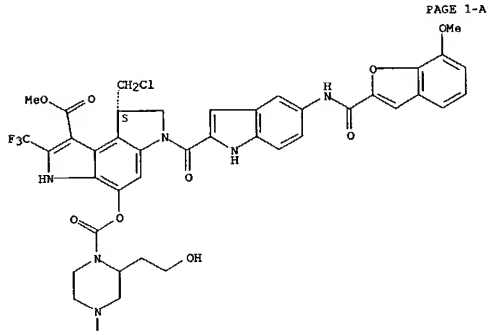
● HCl

RN 211053-37-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[2-(2-hydroxyethyl)-4-methyl-1-piperazinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



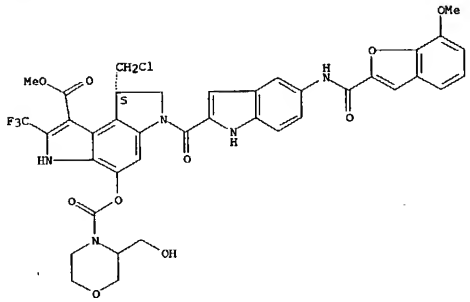
PAGE 2-A

● HCl

RN 211053-38-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

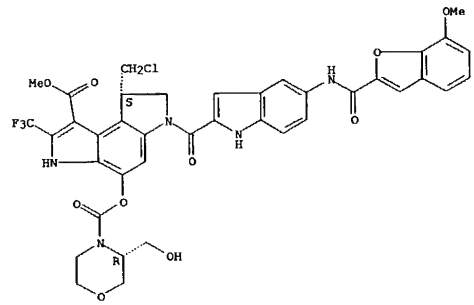
Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 211053-39-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(3R)-3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



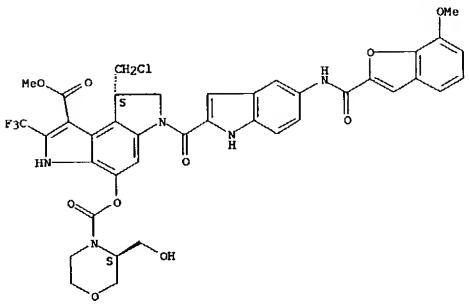
L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 211053-40-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[[(3S)-3-(hydroxymethyl)-4-morpholinyl]carbonyl]oxy]-6-[[5-

[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
(trifluoromethyl)-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

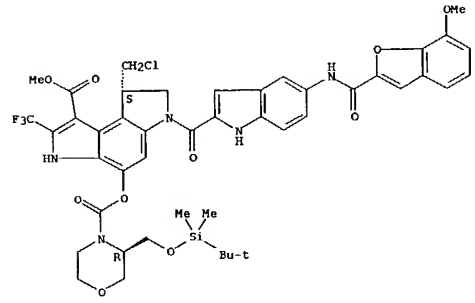


RN 211053-41-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[(3S)-
3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-
morpholinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-2-

benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

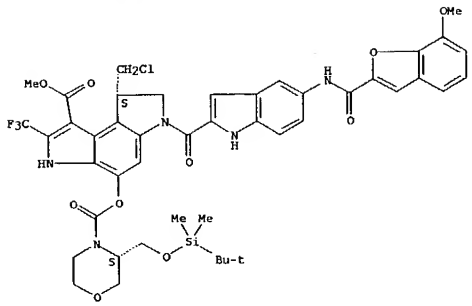
Absolute stereochemistry.

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 32 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 211053-42-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-4-[[[(3R)-
3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-
morpholinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-2-

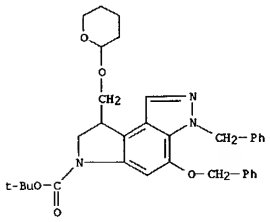
benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,
methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

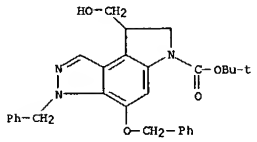
L14 ANSWER 33 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:329287 CAPLUS
DN 129:67620
TI Synthesis, solvolytic stability and cytotoxicity of a modified
derivative
of CPzI, a pyrazole analog of the alkylation subunit of the antitumor
agent CC-1065: effect of the nitrogen substitution on the functional
reactivity
AU Baraldi, Pier Giovanni; Cacciari, Barbara; Guiotto, Andrea; Romagnoli,
Romeo; Spalluto, Giampiero; Zaid, Abdel Naser; Capolongo, Laura;
Cozzi,
Paolo; Geroni, Cristina; Mongelli, Nicola
CS Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara,
44100, Italy
SO Farmaco (1997), 52(12), 717-723
CODEN: FRMCE8; ISSN: 0014-827X
PB Societa Chimica Italiana
DT Journal
LA English
AB The synthesis and the comparative preliminary biol. evaluation of a
new
pyrazole analog, (±)-5-benzyl-2-(tert-butyloxycarbonyl)-1,2,8,8a-
tetrahydrocyclopropa[c]pyrazo[4,3-e]indol-4-one (I), of the CC-1065
alkylating unit (CPI) are described. I showed low cytotoxicity
against
L1210 murine leukemia (IC50 3064 nM) with respect to reference
compound, but
contrarily to literature data, was found to be more stable to
solvolysis
than the natural derivative (±)-N-Boc-CPI (pH 3, t1/2 = 212 h vs. 37
h).
The results of such investigation showed that alkylation of the
pyrazole
nitrogen caused a loss of cytotoxic activity in vitro against tumor
cells.
This exptl. observation allowed us to confirm the importance of free
N-H
for the anticellular activity.
IT **209050-33-9P 209050-34-0P 209050-35-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(synthesis and cytotoxicity of pyrazole analog of antitumor agent
CC-1065)
RN 209050-33-9 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-4-

(phenylmethoxy)-3-(phenylmethyl)-8-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-
, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 33 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

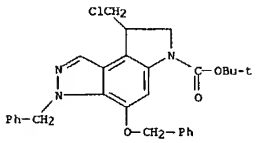


RN 209050-34-0 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-3-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 209050-35-1 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-3-(phenylmethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 33 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 34 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:197505 CAPLUS
DN 128:243876
TI Intermediates for the preparation of duocarmycin SA and its derivatives
thereof, and process for the production of the intermediates
IN Fukuda, Yasumichi; Terashima, Shiro
PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center; ...
Fukuda, Yasumichi; Terashima, Shiro
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9812197	A1	19980326	WO 1997-JP2207	19970626
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, SG, SI, SK, TR, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 10087666	A2	19980407	JP 1996-246097	19960918
AU 9732749	A1	19980414	AU 1997-32749	19970626
EP 937726	A1	19990825	EP 1997-928473	19970626
EP 937726	B1	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1230960	A	19991006	CN 1997-198004	19970626
CN 1090632	B	20020911		
AT 234304	E	20030315	AT 1997-928473	19970626
US 6066742	A	20000523	US 1999-254515	19990309
KR 2000036211	A	20000626	KR 1999-702272	19990317
PRAI JP 1996-246097	A	19960918		
WO 1997-JP2207	W	19970626		

OS CASREACT 128:243876; MARPAT 128:243876
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

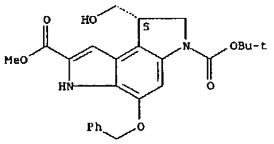
AB Indole derivs. I [R1, R2, R3 = protecting group; R4 = C1-6 alkyl, benzyl] undergo oxidative cyclization to give title compds. II. Thus, indoline III was reacted with Me-CHBr-COOMe in benzene containing 1,8-bis(dimethylamino)naphthalene to give 97% (3S)-I [R1 = BOC, R2 = acetyl, R3 = benzyl, R4 = Me], which was oxidized with MnO2 in N,N-dimethylacetamide contg. p-nitrobenzoic acid and palladium acetate to give 23% the title compd. (-)-(S)-II [R1-R4 same as above].

L14 ANSWER 34 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **197657-12-8P 197657-13-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of intermediates for preparation of duocarmycin SA and its derivs.)

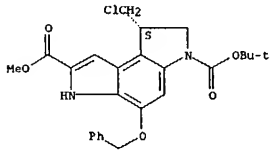
RN 197657-12-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 197657-13-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

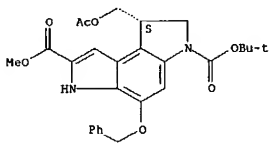


IT **197657-11-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of intermediates for preparation of duocarmycin SA and its derivs.)

RN 197657-11-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

L14 ANSWER 34 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

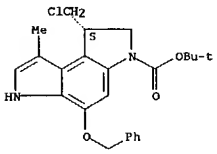
Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:191565 CAPLUS
DN 128:270457
TI Novel synthesis of optically active CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin), U-77,779 (bizelesin), KW-2189, and DU-86
AU Fukuda, Yasumichi; Furuta, Hirosuke; Shiga, Futoshi; Asahina, Yoshikazu; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Tochigi, 329-01, Japan
SO Heterocycles (1997), 45(12), 2303-2308
CODEN: HTCYAM; ISSN: 0385-5414
PB Japan Institute of Heterocyclic Chemistry
DT Journal
LA English
OS CASREACT 128:270457
AB The title syntheses were achieved by the method featuring oxidative cyclization of the enamino esters [(S)-13 and (S)-24] derived from the 5-aminoindoline [(S)-12], acylation with various structural types of indole-2-carboxylic acids, and formation of cyclopropapyrroloindole moieties.
IT **110314-50-6P 112836-67-6P 156295-31-7P**
156295-32-8P 156295-33-9P 176685-39-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis of CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin), U-77,779 (bizelesin), KW-2189, and DU-86)
RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI)
(CA INDEX NAME)

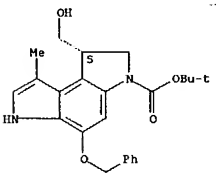
Absolute stereochemistry.



RN 112836-67-6 CAPLUS

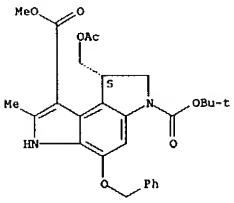
L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 156295-31-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

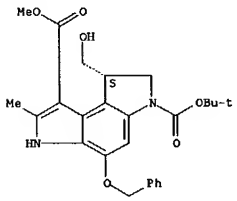
Absolute stereochemistry.



RN 156295-32-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

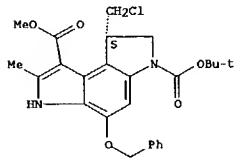
Absolute stereochemistry.

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 156295-33-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

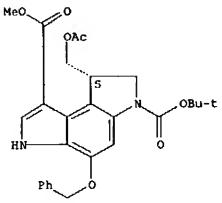
Absolute stereochemistry.



RN 176685-39-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

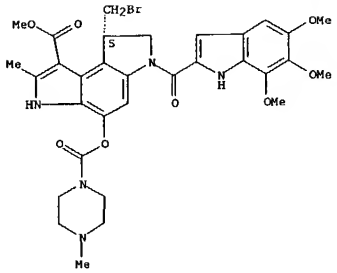
L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **154889-68-6P**, KW-2189
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of CC-1065, U-73,975 (adozelesin), U-80,244 (carzelesin),
U-77,779 (bizelesin), KW-2189, and DU-86)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 35 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

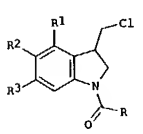


RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

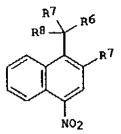
L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:180874 CAPLUS
DN 128:243950
TI Preparation of indolylcarbonylbenzindoles and analogs as antitumor prodrugs
IN Denny, William Alexander; Tercel, Moana; Atwell, Graham John
PA Auckland Division Cancer Society of New Zealand Inc., N. Z.; Denny, William Alexander; Tercel, Moana; Atwell, Graham John
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9811101	A2	19980319	WO 1997-NZ117	19970912
	WO 9811101	A3	19980423		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744039	A1	19980402	AU 1997-44039	19970912
	AU 721037	B2	20000622		
	EP 938474	A2	19990901	EP 1997-942316	19970912
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 334344	A	20000825	NZ 1997-334344	19970912
	JP 2000517292	T2	20001226	JP 1997-537492	19970912
	US 6130237	A	20001010	US 1999-266966	19990312
PRAI	GB 1996-19082	A	19960912		
	GB 1997-7394	A	19970410		
	WO 1997-NZ117	W	19970912		

OS MARPAT 128:243950
GI



I

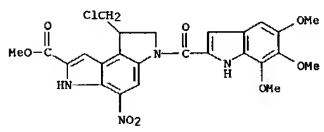


II

L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB Title compds. [I; R = heterocyclyl(ethenyl); R1R2 = CH:CHCH:CH, CH:CR5NH, etc.; R3 = NO2, NH2, NHOH, SH, alkylthio, etc.; R4 = halo, OSO2H, alkylsulfonyloxy, etc.; R5 = CO2H, alkoxycarbonyl, etc.] were prepared for use in, e.g., ADEPT therapy. Thus, naphthylmalonate II (R6 = H, R7 = CON3, R7 = R8 = CO2Me) (preparation given) was cyclized to give II (R6R7 = CONH, R7 = R8 = CO2Me) which was converted in 5 steps to II (R6R7 = CH2NCO2CMe3, R7 = CH2Cl, R8 = H). The latter was deprotected and the product N-acylated by 5,6,7-trimethoxyindole-2-carboxylic acid to give I (R = 5,6,7-trimethoxyindol-2-yl, R1R2 = CH:CHCH:CH, R3 = NO2, R4 = Cl). Data for biol. activity of I were given.

IT **204915-56-0P 204915-58-2P 204915-59-3P**
204915-60-6P 204915-61-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolylcarbonylbenzindoles and analogs as antitumor prodrugs)
RN 204915-56-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

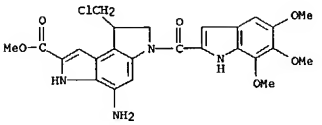


RN 204915-58-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-amino-8-(chloromethyl)-,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, compd. with ethyl acetate (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 204915-57-1
CMF C25 H25 Cl N4 O6

L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



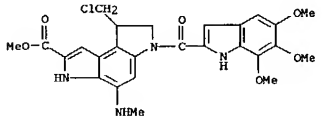
CM 2

CRN 141-78-6
CMF C4 H8 O2

Et—O—Ac

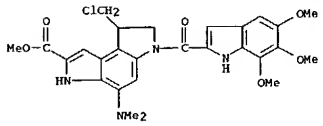
RN 204915-59-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-(methylamino)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

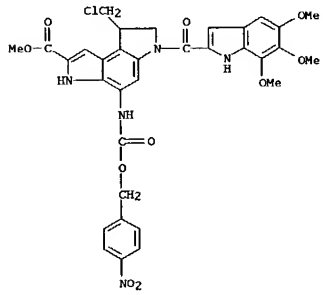


RN 204915-60-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-(dimethylamino)-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

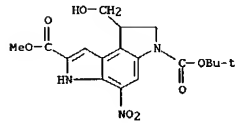


RN 204915-61-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-nitrophenyl)methoxy]carbonyl]amino]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

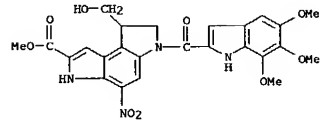


IT **204916-10-9P 204916-11-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of indolylcarbonylbenzindoles and analogs as antitumor prodrugs)
RN 204916-10-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-nitro-, 6-(1,1-dimethylethyl) 2-methyl

L14 ANSWER 36 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ester (9CI) (CA INDEX NAME)



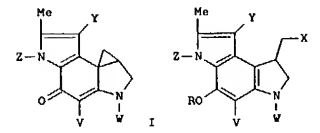
RN 204916-11-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-nitro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



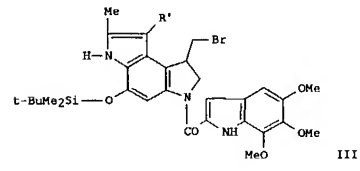
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:175925 CAPLUS
DN 128:243875
TI Preparation of antitumor DC-89 derivatives
IN Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Okabe, Masami
PA Kyowa Hakko Kogyo Co., Ltd., Japan; Amishiro, Nobuyoshi; Saito, Hiromitsu; Okamoto, Akihiko; Okabe, Masami
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809966	A1	19980312	WO 1997-JP3089	19970903
	W: AU, BG, BR, CA, CN, CZ, HU, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9741345	A1	19980326	AU 1997-41345	19970903
PRAI	JP 1996-232723		19960903		
	WO 1997-JP3089		19970903		

OS MARPAT 128:243875
GI



I II



III

AB DC-89 derivs. I and II [Y = H, halo, (un)substituted alkyl, COR1, OR2, SR3, etc.; R1 = H, (un)substituted alkyl, (un)substituted aralkyl, etc.;

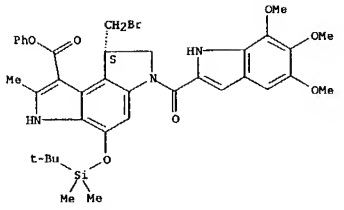
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
R2 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted
aryl, etc.; R3 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted aryl, (un)substituted heterocyclyl; W = H, acyl such as
substituted acryloyl, etc.; Z = H, (un)substituted alkyl, (un)substituted
alkenyl, (un)substituted aryl, COR9 , etc.; R9 = H, acyl, silyl; V = H,
halo, NO2, etc.; X = Cl, Br; R = H, OH, alkoxy, aryl, etc.] and their pharmaceutically acceptable salts are prepd. E.g., the title compd. III
[R' = Me] was prepd. in 56% yield by redn. of III [R' = COOMe] with DIBAL-H in THF. In an in vitro study, II [Y = CH2NMe2, R = V = Z = H, X =
Cl, W = 5,6,7-trimethoxy-1H-indol-2-ylcarbonyl] HCl (also prepd.) had an
IC50 of 0.28 nM against HeLaS3 tumor cells.

IT **205050-82-4P 205050-84-6P 205050-96-0P**
205051-05-4P 205051-09-8P 205051-11-2P
205051-13-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(preparation of antitumor DC-89 derivs.)

RN 205050-82-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenyl ester, (S)- (9CI) (CA INDEX NAME)

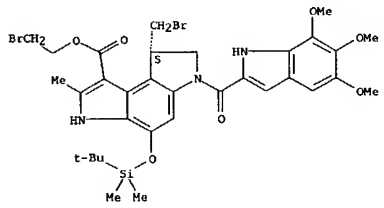
Absolute stereochemistry.

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



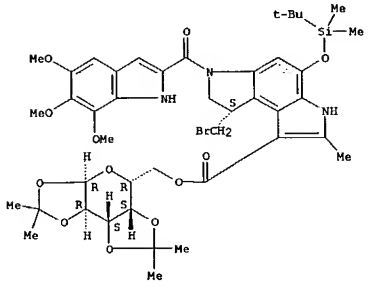
RN 205050-84-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-bromoethyl ester, (8S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



RN 205050-96-0 CAPLUS
CN α-D-Galactopyranose, 1,2:3,4-bis-O-(1-methylethylidene)-, (8S)-8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-
tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrole-1-carboxylate (9CI) (CA INDEX NAME)

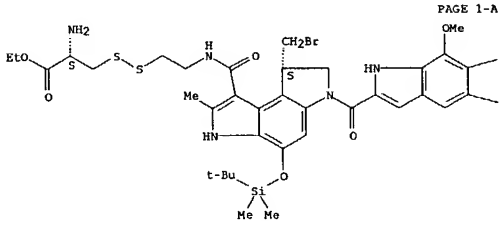
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.



RN 205051-05-4 CAPLUS
CN L-Alanine, 3-[[2-[[[(8S)-8-(bromomethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-1-yl]carbonyl]amino]ethyl]dithio]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

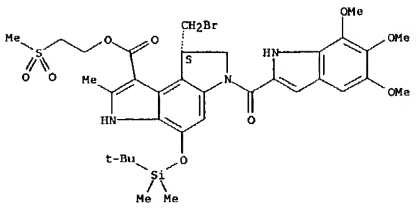
RN 205051-09-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 5-hydroxy-1,2-dithian-4-yl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 205051-11-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-(methylsulfonyl)ethyl ester, (8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

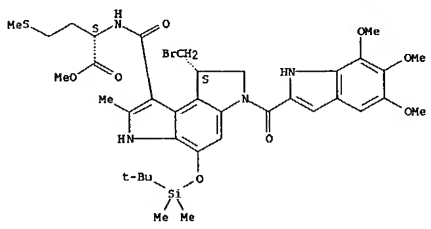
L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 205051-13-4 CAPLUS
CN L-Methionine, N-[[(8S)-8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-1-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



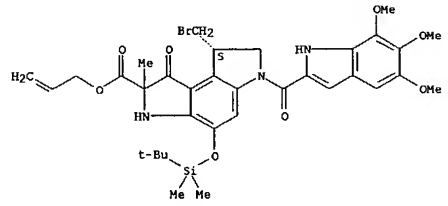
IT **129953-15-7 177958-19-9 205051-55-4**
205051-56-5 205051-57-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor DC-89 derivs.)
RN 129953-15-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)-(9CI)
(CA INDEX NAME)

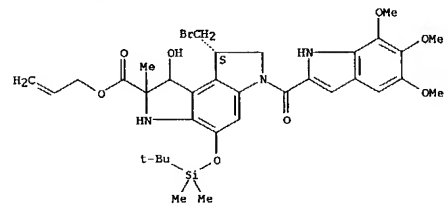
Absolute stereochemistry.



RN 205051-56-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



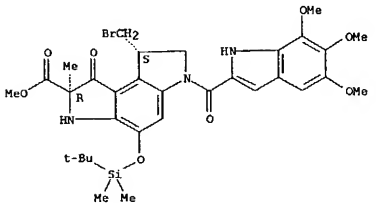
RN 205051-57-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester, (8S)- (9CI) (CA

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-(9CI)
(CA INDEX NAME)

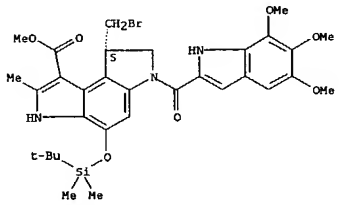
Absolute stereochemistry.



RN 177958-19-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

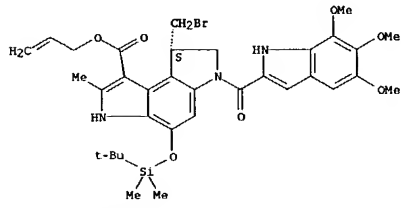
Absolute stereochemistry.



RN 205051-55-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

L14 ANSWER 37 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

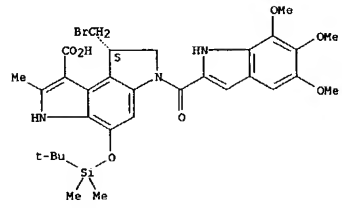
Absolute stereochemistry.



IT **205051-58-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of antitumor DC-89 derivs.)
RN 205051-58-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, (8S)- (9CI) (CA INDEX NAME)

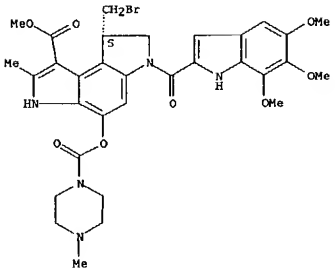
Absolute stereochemistry.



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 38 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:791611 CAPLUS
DN 128:110513
TI In vitro enhancement of antitumor activity of a water-soluble duocarmycin derivative, KW-2189, by caffeine-mediated DNA-repair inhibition in human lung cancer cells
AU Ogasawara, Hayato; Nishio, Kazuto; Ishida, Tomoyuki; Arioka, Hitoshi; Fukuoka, Kazuya; Saijo, Nagahiro
CS Pharmacology Division, National Cancer Center Research Institute, Tokyo, 104, Japan
SO Japanese Journal of Cancer Research (1997), 88(11), 1033-1037
CODEN: JJCREP; ISSN: 0910-5050
PB Japanese Cancer Association
DT Journal
LA English
AB Duocarmycins, including KW-2189, bind in the minor groove of double-stranded DNA at A-T-rich sequences, followed by covalent bonding with N-3 of adenine in preferred sequences. We examined the effect of DNA-repair modulators, such as caffeine and aphidicolin, on the cytotoxicity of duocarmycins towards human lung cancer cells, as determined by dye formation assay. Caffeine (0.5 or 1 mM), but not aphidicolin, enhanced the growth-inhibitory activity of KW-2189, DU-86, and duocarmycin SA. Caffeine inhibited repair of DNA strand breaks induced by KW-2189, as assayed by the alkaline elution technique. This suggests that duocarmycin-induced DNA strand breaks, which are potentially lethal to cells, are repaired through a caffeine-sensitive pathway.
IT **154889-68-6**, KW-2189
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro enhancement of antitumor activity of a water-soluble duocarmycin derivative, KW-2189, by caffeine-mediated DNA-repair inhibition in human lung cancer cells)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

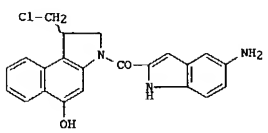


RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 39 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:783786 CAPLUS
DN 128:48468
TI Preparation of DNA-binding glucuronide indoles immuno-conjugates as antitumors
IN Wang, Yuqiang; Wright, Susan C.; Larrick, James W.
PA Panorama Research, Inc., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

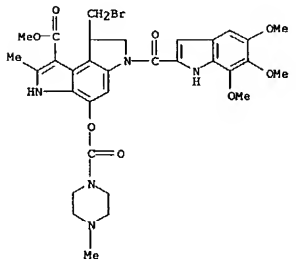
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9744000	A2	19971127	WO 1997-US9055	19970522
	WO 9744000	A3	19971231		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5843937	A	19981201	US 1996-652883	19960523
	AU 9732170	A1	19971209	AU 1997-32170	19970522
	EP 918752	A2	19990602	EP 1997-927798	19970522
	R: AT, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
	CN 1219841	A	19990616	CN 1997-194862	19970522
	JP 2000511893	T2	20000912	JP 1997-542898	19970522
PRAI	US 1996-652883	A	19960523		
	WO 1997-US9055	W	19970522		

OS MARPAT 128:48468
GI



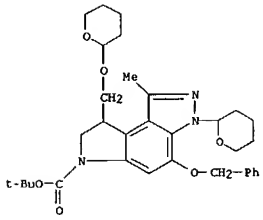
I

AB The present invention relates to novel DNA alkylating agents and the prodrugs of these agents which are useful as antitumors and DNA labeling agents. The compds. are hydroxydihydrobenzindole oligopeptides and prodrugs thereof wherein the monomeric constituents are derived from monocyclic, or bicyclic heterocyclic arom. residues. Thus, indole I was prepd. and tested for its antitumor activity with cytotoxicity (IC50 = 0.09 nM).
IT **134106-78-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of DNA-binding glucuronide hydroxydihydrobenzindole oligopeptides immuno-conjugates as antitumors)
RN 134106-78-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

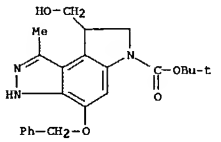


L14 ANSWER 40 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:716591 CAPLUS
DN 128:57126
TI Synthesis, cytotoxicity, antitumor activity and sequence selective binding
of two pyrazole analogs structurally related to the antitumor agents U-71,184 and adozelesin
AU Baraldi, Pier Giovanni; Cacciari, Barbara; Romagnoli, Romeo; Spalluto,
Giampiero; Gambari, Roberto; Bianchi, Nicoletta; Passadore, Marco; Ambrosino, Piera; Mongelli, Nicola; Cozzi, Paolo; Geroni, Cristina
CS Dipartimento di Scienze Farmaceutiche, Ferrara, I-44100, Italy
SO Anti-Cancer Drug Design (1997), 12(7), 555-576
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
AB Two pyrazole analogs structurally related to the antitumor agents adozelesin and U-71,184 resp. were synthesized. By using a polymerase
chain reaction approach, both compds. show selective binding to A + T rich
sequences exactly as reference compound U-71,184. In in vitro assays, against
L1210 cell lines, both derivs. showed cytotoxicity in the pM range, values
comparable with the natural target compound (+)-CC-1065. The most active
compound showed very high antitumor activity in mice implanted with L1210
cells (ILS% 363).
IT **187034-23-7P 187034-24-8P 187034-25-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and antitumor activity and DNA binding of pyrazole analogs
related to U-71,814 and adozelesin)
RN 187034-23-7 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-1-methyl-4-(phenylmethoxy)-3-(tetrahydro-2H-pyran-2-yl)-8-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 40 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

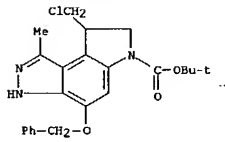


RN 187034-24-8 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)



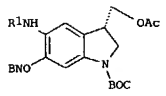
RN 187034-25-9 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 40 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

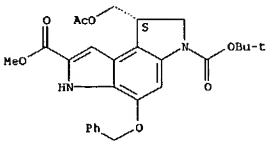
L14 ANSWER 41 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:707375 CAPLUS
DN 127:318803
TI A novel synthesis of (+)-duocarmycin SA
AU Fukuda, Yasumichi; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi, 329-01, Japan
SO Tetrahedron Letters (1997), 38(41), 7207-7208
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 127:318803
GI



AB The title synthesis was achieved in eight steps from (S)-5-aminoindoline
(I)(R1 = H) by a method featuring sequential dehydrogenation, double bond
isomerization, and oxidative cyclization of (S)-5-[(1-methoxycarbonylethyl)amino]indoline (II) [I, R1 = (S)-CH(Me)CO2Me] as the
key steps. The sequential reaction was effected by using MnO2-Pd(OAc)2 as
the oxidizing agent in the presence of an acid catalyst.
IT **197657-11-7P 197657-12-8P 197657-13-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis of (+)-duocarmycin SA)
RN 197657-11-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

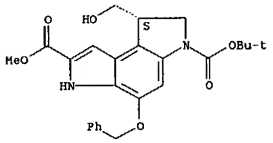
Absolute stereochemistry. Rotation (-).

L14 ANSWER 41 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 197657-12-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

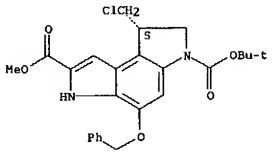
Absolute stereochemistry. Rotation (-).



RN 197657-13-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 41 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



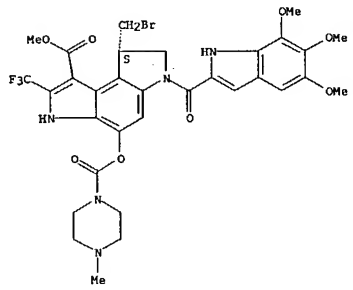
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:468982 CAPLUS
DN 127:185373
TI Synthesis and antitumor activity of novel cyclopropapyrroloindole (CPI) derivatives bearing methoxycarbonyl and trifluoromethyl groups
AU Fukuda, Yasumichi; Furuta, Hirosuke; Shiga, Futoshi; Oomori, Yasuo; Kusama, Yoshie; Ebisu, Hiroyuki; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi, 329-01, Japan
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(13), 1683-1688
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
AB The title synthesis was achieved by employing oxidative cyclization of the enamino ester as a key step. Some of these novel 3-methoxycarbonyl-2-trifluoromethylcyclopropapyrroloindole (MCTFCPI) derivs. were found to exhibit antitumor activity against murine leukemia and murine solid tumors more prominent than that of known CPI derivs.
IT **194361-61-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antitumor activity of cyclopropapyrroloindole derivs. bearing methoxycarbonyl and trifluoromethyl groups)
RN 194361-61-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



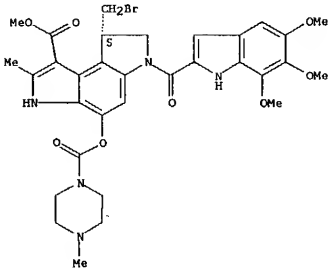
PAGE 2-A

● HCl

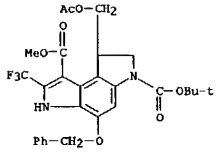
IT **154889-68-6**, KW 2189
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and antitumor activity of cyclopropapyrroloindole derivs. bearing methoxycarbonyl and trifluoromethyl groups)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

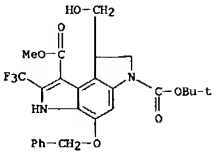


IT **194093-62-4P 194093-63-5P 194093-64-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis and antitumor activity of cyclopropapyrroloindole derivs.
bearing methoxycarbonyl and trifluoromethyl groups)
RN 194093-62-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

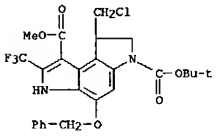


RN 194093-63-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-,

L14 ANSWER 42 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-64-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

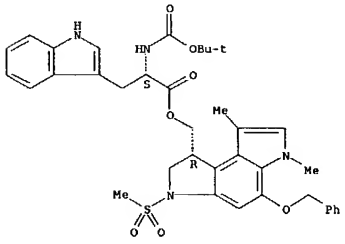


RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

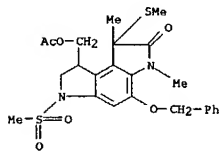
L14 ANSWER 43 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:436161 CAPLUS
DN 127:130933
TI Sequence and Structure Dependence of the Hybridization-Triggered Reaction
of Oligonucleotides Bearing Conjugated Cyclopropapyrroloindole
AU Lukhtanov, Eugeny A.; Kutyavin, Igor V.; Gorn, Vladimir V.; Reed, Michael
W.; Adams, A. David; Lucas, Deborah D.; Meyer, Rich B., Jr.
CS Epoch Pharmaceuticals Inc., Bothell, WA, 98021, USA
SO Journal of the American Chemical Society (1997), 119(27), 6214-6225
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB Oligodeoxyribonucleotides (ODNs) with conjugated reactive groups are potential sequence-specific gene inactivating agents. The antitumor antibiotic CC-1065 binds preferably in the minor groove of A-T-rich sites
of double-stranded DNA, and the cyclopropapyrroloindole (CPI) subunit of
the drug alkylates adenines at their N3 position. Pure enantiomeric (+)-
and (-)-CPI and its N5-Me homolog (MCPI) were synthesized and conjugated
to an ODN. These conjugates were evaluated for their ability to alkylate
a target containing a duplex region immediately adjacent to a single-stranded
complementary binding region for the ODN conjugate. The conjugates demonstrated excellent stability in physiol. conditions and stereospecific, hybridization-triggered alkylation of the synthetic ODN
targets. The dependence of the reaction rates on sequence of the duplex
target region was in accord with the predicted minor groove binding of the
conjugated CPI. The reactivity was highly dependent on the structure of
the crosslinking group. Natural (+)-enantiomers alkylate 10-20 times faster than the corresponding (-)-enantiomers. Regiospecificity of the
alkylation reaction is conferred by the length of the spacer arm. N5-Methylation of the CPI moiety suppresses the reactivity by a factor of
3-5. Addition of a 1,2-dihydro-3H-pyrrolo[3,2-e]indole-7-carboxylate (DPI)
binding subunit of CC-1065 between CPI or MCPI residues and an ODN results
in a significant enhancement of the reactivity which is especially pronounced
for (-)-enantiomers. The main products of sequence-specific alkylation
were determined for complexes with the most efficient reactions.
IT **192657-43-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclopropapyrroloindole-conjugated oligonucleotide preparation and target

L14 ANSWER 43 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
hybridization-assocd. alkylation)
RN 192657-43-5 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [(1R)-1,2,3,6-tetrahydro-6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



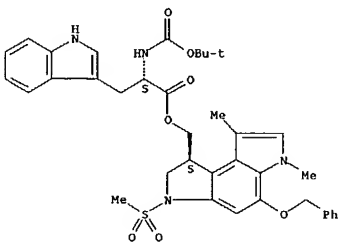
IT **192657-40-2P 192657-42-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction; cyclopropapyrroloindole-conjugated oligonucleotide preparation and target hybridization-associated alkylation)
RN 192657-40-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-1,3-dimethyl-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)



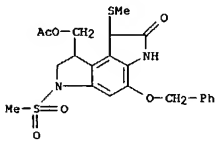
RN 192657-42-4 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [(1S)-1,2,3,6-tetrahydro-

L14 ANSWER 43 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
6,8-dimethyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester (9CI) (CA INDEX NAME)

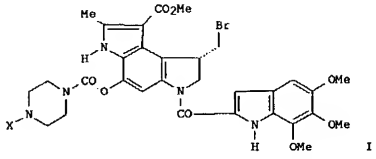
Absolute stereochemistry.



IT **112089-53-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; cyclopropapyrroloindole-conjugated oligonucleotide preparation
and target hybridization-associated alkylation)
RN 112089-53-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)-(9CI) (CA
INDEX NAME)



L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:404887 CAPLUS
DN 127:108790
TI The synthesis of [3H]KW-2189, a novel active antitumor antibiotic
AU Nagamura, Satoru; Kinugawa, Masahiko; Ogasa, Takehiro; Saito, Hiromitsu
CS Kyowa Hakko Kogyo Co. Ltd., Tokyo Research Laboratories, Machida, 194, Japan
SO Journal of Labelled Compounds & Radiopharmaceuticals (1997), 39(6), 471-477
CODEN: JLCRD4; ISSN: 0362-4803
PB Wiley
DT Journal
LA English
GI

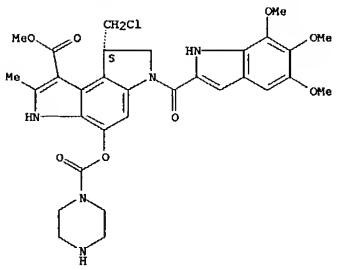


AB The synthesis of [3H]KW-2189 (I, X = C3H3), a novel active antitumor antibiotic, is described. The key intermediate I (X = H) in the synthesis, was synthesized in four steps from duocarmycin B2.
Treatment
of I (X = H) with [3H]methyl iodide in the presence of NaHCO3 in MeOH-Me2CO (1:1) afforded the [3H]KW-2189 with highly specific activity of
86.4 Ci/mmol.
IT **192509-06-1P**
RL: BYP (Byproduct); PREP (Preparation)
(preparation of [3H]KW-2189)
RN 192509-06-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-piperazinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

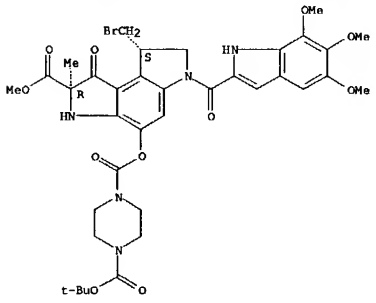
L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **192509-07-2P 192509-08-3P 192509-09-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of [3H]KW-2189)
RN 192509-07-2 CAPLUS
CN 1,4-Piperazinedicarboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-(methoxycarbonyl)-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl 1,1-dimethylethyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

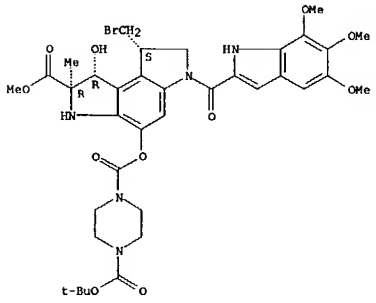
Absolute stereochemistry.

L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192509-08-3 CAPLUS
CN 1,4-Piperazinedicarboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-(methoxycarbonyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl 1,1-dimethylethyl ester, [1R-(1α,2β,8α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

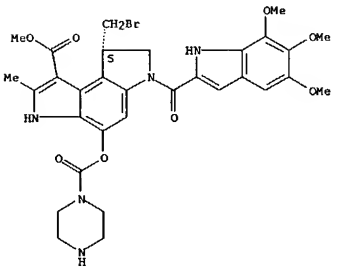


L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 192509-09-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[(1-piperazinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H
-

indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

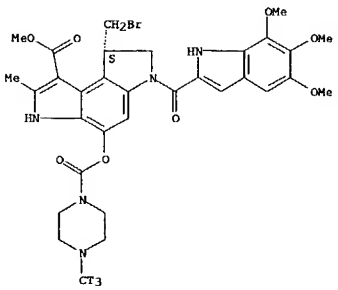
Absolute stereochemistry.



IT **192509-10-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [3H]KW-2189)
RN 192509-10-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[[4-(methyl-t3)-1-piperazinyl]carbonyl]oxy]-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)-
(9CI) (CA
INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 44 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

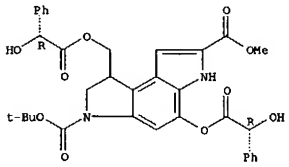


L14 ANSWER 45 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:324291 CAPLUS
DN 127:12962
TI Duocarmycin SA shortened, simplified, and extended agents: a
systematic
examination of the role of the DNA binding subunit
AU Boger, Dale L.; Hertzog, Donald L.; Bollinger, Bernd; Johnson,
Douglas S.;
Cai, Hui; Goldberg, Joel; Turnbull, Philip
CS Department of Chemistry, Scripps Research Institute, La Jolla, CA,
92037,
USA
SO Journal of the American Chemical Society (1997), 119(21), 4977-4986
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The examination of shortened, simplified, and extended analogs of
duocarmycin
SA are described and constitute a detailed study of the role of
linked DNA
binding subunit. In addition to enhancing the DNA binding affinity
and
selectivity through minor groove noncovalent contacts, the studies in
conjunction with those of the accompanying article illustrate that an
extended rigid N2 amide substituent is required for catalysis of the
DNA
alkylation reaction. This activation for DNA alkylation is
independent of
pH, and we propose it results from a binding-induced conformational
change
in the agents which increases their inherent reactivity. The ground
state
destabilization of the substrate results from a twist in the linking
amide
that disrupts the vinylogous amide stabilization of the alkylation
subunit
and activates the agent for nucleophilic addition This leads to
preferential
activation of the agents for DNA alkylation within the narrower,
deeper
AT-rich minor groove sites where the inherent twist in the linking
amide
and helical rise of the bound conformation is greatest. Thus,
shape-selective recognition (preferential AT-rich noncovalent
binding) and
shape-dependent catalysis (induced twist in linking N2 amide)
combine to
restrict SN2 alkylation to accessible adenine N3 nucleophilic sites
within
the preferred binding sites. Addnl. ramifications of this DNA
binding-induced conformational change on the reversibility of the DNA
alkylation reaction are discussed. The results of the study
illustrate
the importance of the C5' methoxy group and the C6 Me ester of
duocarmycin
SA, and a previously unrecognized role for these substituents is
proposed.

L14 ANSWER 45 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **190060-22-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(duocarmycin SA shortened, simplified, and extended agents: a
systematic examination of the role of the DNA binding subunit)
RN 190060-22-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

7,8-dihydro-4-[(hydroxyphenylacetyl)oxy]-8-[[(hydroxyphenylacetyl)oxy]meth
yl]-, 6-(1,1-dimethylethyl) 2-methyl ester, [4(R),8(R)]-[partial]-
(9CI)
(CA INDEX NAME)

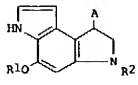
Absolute stereochemistry.



L14 ANSWER 46 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:262265 CAPLUS
DN 126:277505
TI Preparation of 8-methylpyrroloindole derivatives as antibiotics and antitumor agents
IN Fukuda, Yasuji; Furuta, Kosuke; Terajima, Atsuro
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 09067374	A2	19970311	JP 1995-223056	19950831
PRAI JP 1995-223056		19950831		

OS MARPAT 126:277505
GI

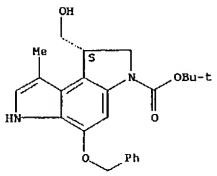


I

AB The title compds. [I; Y = Me; R1 = protecting group of amino; A = CH2X1;
X1 = halo, OH, OSO2R4; R4 = alkyl, aralkyl, (un)substituted aryl, OR5; R2,
R5 = protecting group of OH] are prepared by reduction of I (Y = CO2R3; R3 =
linear or branched C1-6 alkyl; A = CH2X2; X2 = halo, OH, OSO2R4, etc.; R1,
R2 = same as above). I, useful as antibiotics and antitumor agents (no
data) or intermediates thereof, are prepared efficiently and easily. Thus,
I (Y = CO2Me, A = CH2OAc, R1 = tert-butoxycarbonyl, R2 = C6H4CH2) was refluxed with BH3.THF in THF for 19 h and treated with aqueous citric acid to
give the title compound I (Y = Me, A = CH2OH, R1, R2 = same as above).
IT **112836-67-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-methylpyrroloindole derivs. as antibiotics and antitumor

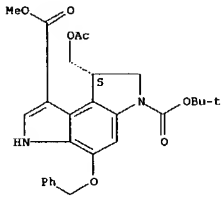
agents)
RN 112836-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



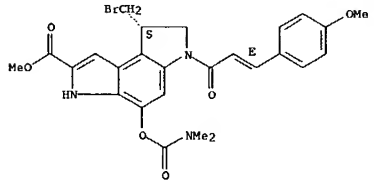
IT **176685-39-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 8-methylpyrroloindole derivs. as antibiotics and antitumor
agents)
RN 176685-39-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AN 1997:228843 CAPLUS
DN 126:311725
TI Studies on duocarmycin SA and its derivatives
AU Nagamura, Satoru; Asai, Akira; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd, Machida, 194, Japan
SO Bioorganic & Medicinal Chemistry (1997), 5(3), 623-630
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
AB New duocarmycin SA derivs. have been synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells, and in vivo antitumor
activity against murine sarcoma 180 in mice. The results suggested that
the N,N-dialkylcarbamoyl derivs. bearing the p-methoxy cinnamoyl group,
prepared from duocarmycin SA, showed good in vivo antitumor activities superior to native duocarmycin SA.
IT **152718-07-5P 152718-08-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(antitumor activity, preparation, and structure of duocarmycin SA derivs.)
RN 152718-07-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

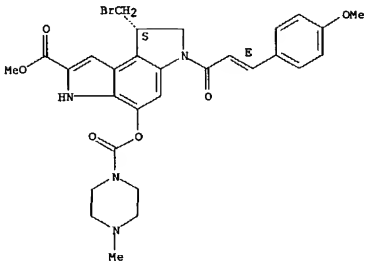
Absolute stereochemistry.
Double bond geometry as shown.



RN 152718-08-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

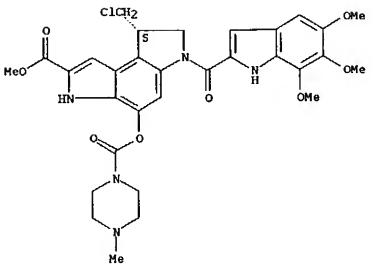


IT **152718-02-0P 152718-03-1P 152718-04-2P**
152718-05-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor activity, preparation, and structure of duocarmycin SA derivs.)
RN 152718-02-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

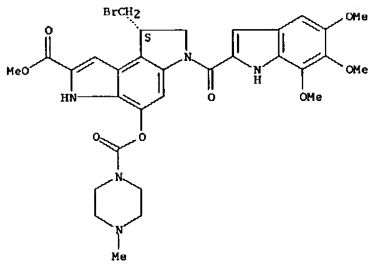
L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-03-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

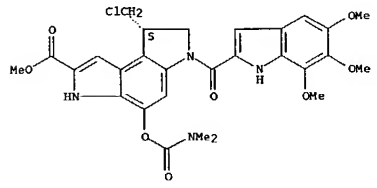
Absolute stereochemistry.



L14 ANSWER 47 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 152718-04-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-

[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

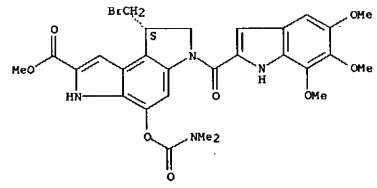
Absolute stereochemistry.



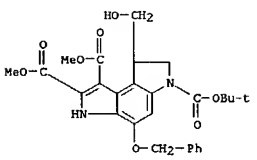
RN 152718-05-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

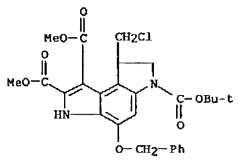


L14 ANSWER 48 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:219845 CAPLUS
DN 126:287689
TI Synthesis and antitumor activity of novel cyclopropapyrroloindole (CPI) derivatives bearing bis(methoxycarbonyl) groups
AU Fukuda, Yasumichi; Oomori, Yasuo; Kusama, Yoshie; Terashima, Shiro
CS Central Research Laboratories, Kyorin Pharmaceutical Co. Ltd., Nogi, 329-01, Japan
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(6), 749-752
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
AB The title synthesis was achieved by employing oxidative cyclization of the enaminodiester prepared by Michael addition of the 5-aminoindoline with di-Me acetylenedicarboxylate, as a key step. Some of these novel bis(methoxycarbonyl)cyclopropapyrroloindole (MC2CPI) derivs. 9c, d and their seco-chlorides 18c, d were found to exhibit prominent cytotoxicity and antitumor activity against P388 murine leukemia.
IT **156905-82-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)
RN 156905-82-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)

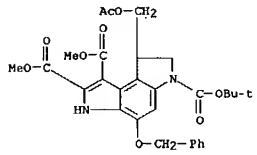


IT **156905-83-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)
RN 156905-83-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 48 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

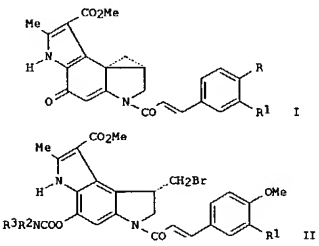


IT **156905-81-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and methanolysis of)
RN 156905-81-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:180818 CAPLUS
DN 126:157310
TI Synthesis and Antitumor Activity of Duocarmycin Derivatives: A-Ring Pyrrole Compounds Bearing Cinnamoyl Groups
AU Nagamura, Satoru; Asai, Akira; Amishiro, Nobuyoshi; Kobayashi, Eiji; Gomi,
Katsushige; Saito, Hiromitsu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Machida, 194, Japan
SO Journal of Medicinal Chemistry (1997), 40(6), 972-979
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
GI



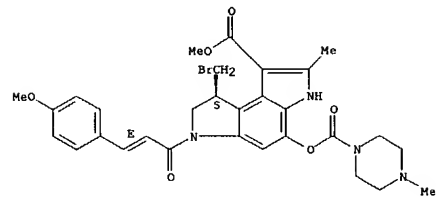
AB A series of DU-86 A segment N6-cinnamoyl derivs I (R = OMe, n-propyloxy,
allyloxy, pentyloxy, 4-methoxybenzyloxy, OH, NMe2, NEt2, Me, Et, NHCO2CMe3, NH2, R1 = H; R = OMe, R1 = 3-azidopropyloxy, 3-dimethylaminopropyloxy, OCH2CO2CMe3, OCH2CO2Me, NEt2, NMe2, NHCO2CMe3,
NH2, 3-aminopropyloxy) were synthesized and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity
against murine sarcoma 180 in mice. The 4'-methoxy- and 4'-BocNH-cinnamoyl derivs. exhibited strong in vitro anticellular activity
compared to the other synthesized compds. The substitution of the 4'-methoxycinnamoyl derivative did not affect the anticellular activity and

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
contributed to an enhancement of water soly. Most of the 8-O-carbamoyl
derivs. II [R1 = H, R3R2N = 4-methylpyrazinyl, 4-piperidinopiperidinyl,
4-(isopropylaminocarbonylmethyl)piperazinyl; R1 = NEt2, NMe2, 3-aminopropyloxy, NH2, OCH2CO2H, R3R2N = 4-methylpyrazinyl] of the 4'-methoxycinnamoyl derivs. displayed remarkably superior in vivo antitumor activity to duocarmycin A or B2. It was noteworthy that these
8-O-carbamoyl derivs. exhibited significant antitumor activity at a wider
range of doses as compared with the A-ring pyrrole derivs. having the trimethoxyindole skeleton in segment B.

IT **186760-19-0P 186760-20-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of DU-86, duocarmycin related, derivs. with A-ring pyrrole compds. bearing cinnamoyl groups)
RN 186760-19-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.
Double bond geometry as shown.

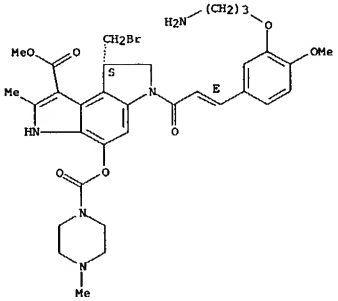


RN 186760-20-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-aminopropoxy)-4-

methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, [S-(E)]-

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

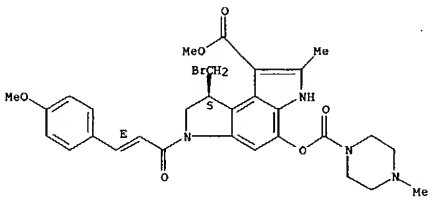


IT **186760-06-5P 186760-07-6P 186760-08-7P**
186760-09-8P 186760-10-1P 186760-11-2P
186760-12-3P 186760-21-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of DU-86, duocarmycin related, derivs. with A-ring pyrrole compds. bearing cinnamoyl groups)
RN 186760-06-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[(2E)-3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



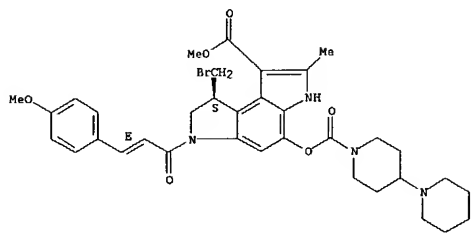
● HCl

RN 186760-07-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[({1,4'-bipiperidin]-1'-

ylcarbonyl)oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-
1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride,
[S-(E)]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

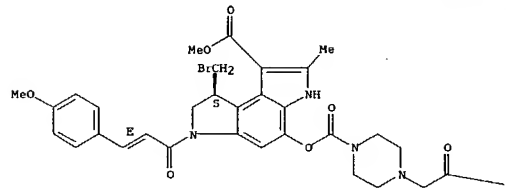
RN 186760-08-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-[2-[(1-
methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl
ester,
monohydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



● HCl

PAGE 1-B

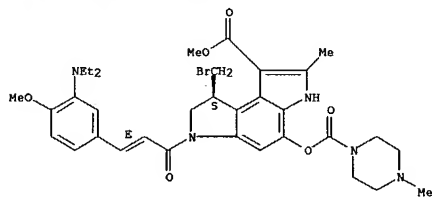
—NHPr-i

RN 186760-09-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



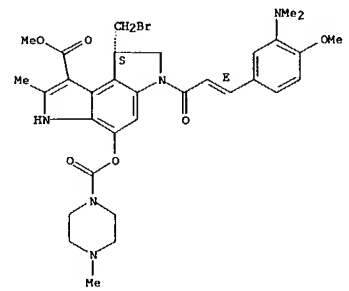
●2 HCl

RN 186760-10-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

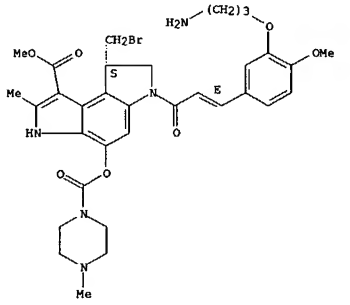
PAGE 2-A

● HCl

RN 186760-11-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-(3-aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

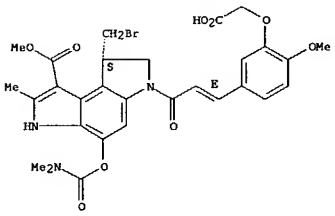
PAGE 1-A



PAGE 2-A

●2 HCl

L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

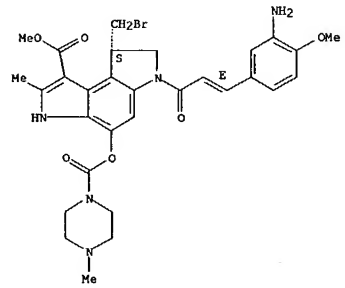


L14 ANSWER 49 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 186760-12-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

●2 HCl

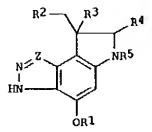
RN 186760-21-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(carboxymethyl)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, [8aS-[2(E),7bS*,8aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

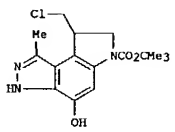
L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:172312 CAPLUS
DN 126:171589
TI Preparation of pyrrolo[3,2-c]indazoles and analogs as antitumor agents
IN Cozzi, Paolo; Baraldi, Pier Giovanni; Beria, Italo; Capolongo, Laura; Spalluto, Giampiero
PA Pharmacia Spa, Italy
SO Brit. UK Pat. Appl., 64 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2300857	A1	19961120	GB 1995-10169	19950519
GB 2300857	B2	19980708		
PRAI GB 1995-10169		19950519		

OS MARPAT 126:171589
GI



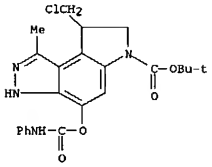
I



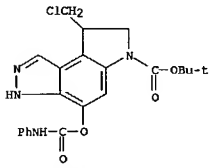
II

AB Title compds. [e.g., I; R1 = H, alkyl, alkanoyl, alkylcarbamoyl, etc.; R2 = halo; R3,R4 = H or alkyl; R5 = H, COR7, (aryl)hydrocarbyl, etc.; R7 = (aryl)hydrocarbyl, alkoxy, etc.; Z = N or CR; R = H or alkyl] were prepared as antitumor agents (no data). Thus, 4-formyl-3-methylpyrazole (preparation given) was converted in 15 steps to title compound II.
IT **187033-75-6P 187033-76-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolo[3,2-c]indazoles and analogs as antitumor agents)
RN 187033-75-6 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-[[(phenylamino)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

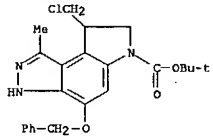


RN 187033-76-7 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-[[(phenylamino)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

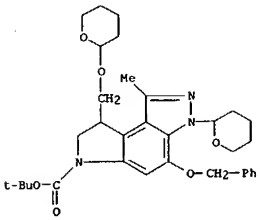


IT **187034-23-7P 187034-24-8P 187034-25-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of pyrrolo[3,2-c]indazoles and analogs as antitumor agents)
RN 187034-23-7 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-1-methyl-4-(phenylmethoxy)-3-(tetrahydro-2H-pyran-2-yl)-8-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

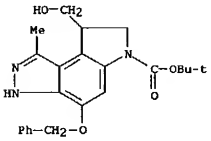
L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 50 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

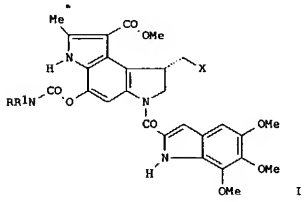


RN 187034-24-8 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)



RN 187034-25-9 CAPLUS
CN Pyrrolo[3,2-e]indazole-6(3H)-carboxylic acid, 8-(chloromethyl)-7,8-dihydro-1-methyl-4-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:596991 CAPLUS
DN 125:328342
TI Synthesis and antitumor activity of duocarmycin derivatives: modification
of segment A of duocarmycin B2
AU Nagamura, Satoru; Asai, Akira; Kanda, Yutaka; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Tokyo, 194, Japan
SO Chemical & Pharmaceutical Bulletin (1996), 44(9), 1723-1730
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
GI

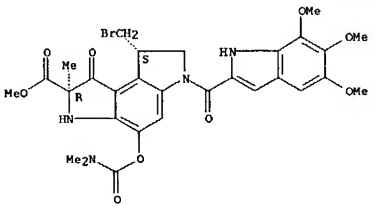


AB Several A-ring pyrrole derivs. of duocarmycin B2, e.g. I (RR1N = Me2N, 4-Me-piperazinyl, piperidinyl, pyrrolidinyl, X = Br, Cl), were synthesized
from the 3-hydroxy compds. by utilizing an interesting acid-catalyzed rearrangement, their anticellular activity was preliminarily evaluated by
assays of growth inhibition of HeLa S3 cells (in vitro) and antitumor activity against murine sarcoma 180 (in vivo). The 8-O-N,N-dialkylcarbamoyl derivs. of the A-ring pyrrole compound showed remarkably
potent in vivo antitumor activity, superior to that of duocarmycin B2. These derivs. were subjected to further biol. evaluation. They exhibited
potent antitumor activity toward murine solid tumors including M5076 sarcoma, B-16 melanoma and Colon 26 adenocarcinoma. Their most noteworthy
feature was their efficacy against various human xenografts including LC-6
(lung), St-4 (stomach), and Co-3 (colon).
IT **171599-25-0 171599-29-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(synthesis and antitumor activity of duocarmycin derivs.)

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 171599-25-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-
[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(2R-trans)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

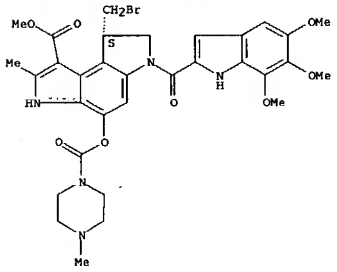


RN 171599-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1
-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

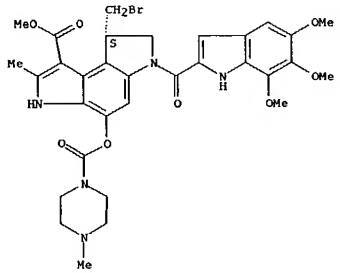


RN 160819-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,
(8S)-
(9CI) (CA INDEX NAME)

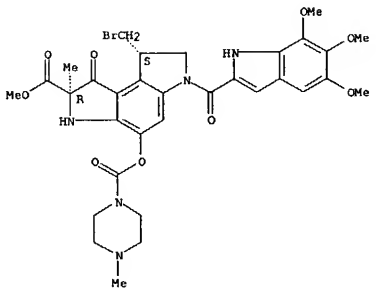
Absolute stereochemistry.

PAGE 1-A



L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

● HCl

IT **154889-68-6P 160819-28-3P 177958-19-9P**
177958-20-2P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation);
BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of duocarmycin derivs.)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

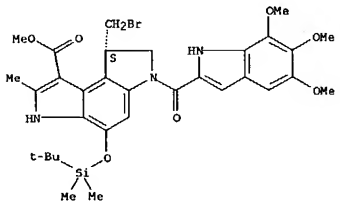
PAGE 2-A

● HBr

RN 177958-19-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

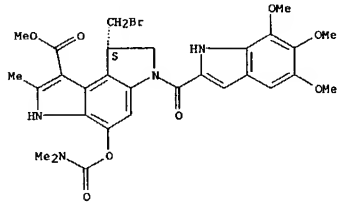
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.



RN 177958-20-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

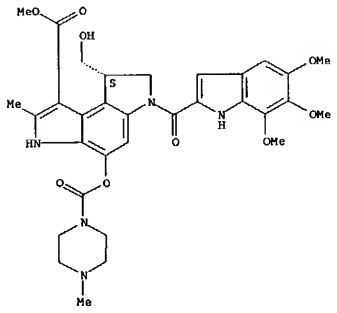
Absolute stereochemistry.



L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **154715-68-1P 183240-24-6P 183240-25-7P**
183240-26-8P 183240-27-9P 183240-28-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of duocarmycin derivs.)
RN 154715-68-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

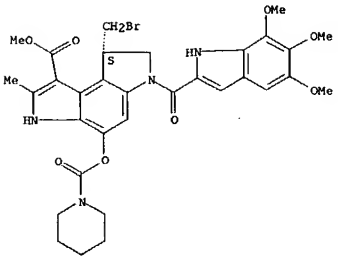
Absolute stereochemistry.



RN 183240-24-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

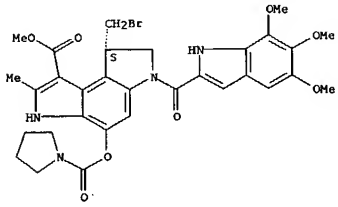
Absolute stereochemistry.

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 183240-25-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

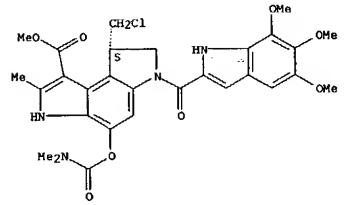
Absolute stereochemistry.



RN 183240-26-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

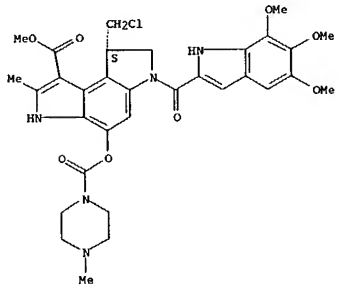
Absolute stereochemistry.



RN 183240-27-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



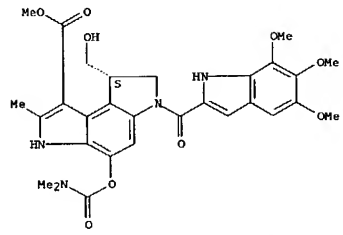
L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HCl

RN 183240-28-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

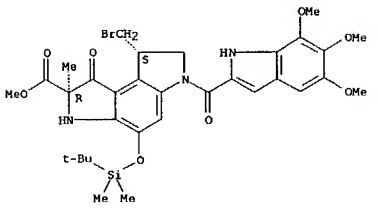
Absolute stereochemistry.



IT **129953-15-7P 129953-17-9P 183240-30-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of duocarmycin derivs.)
RN 129953-15-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

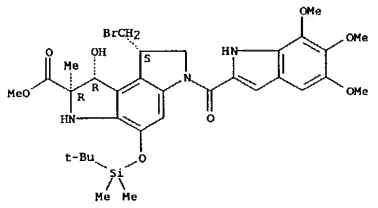
L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 129953-17-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(1R,2R,8S)-
(9CI) (CA INDEX NAME)

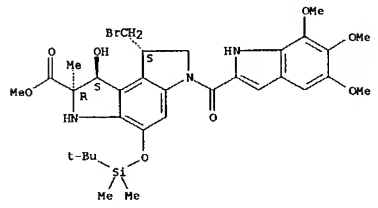
Absolute stereochemistry.



RN 183240-30-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

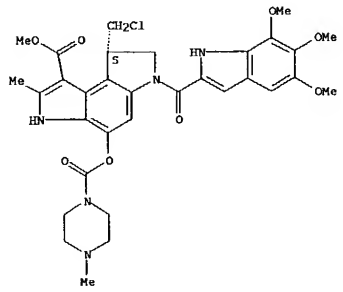
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA
INDEX
NAME)

L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 51 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.

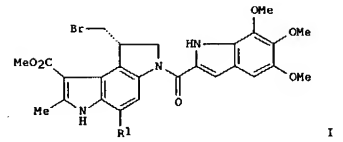


IT **183388-25-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and antitumor activity of duocarmycin derivs.)
RN 183388-25-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-4-[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(1R,2S,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:572393 CAPLUS
DN 125:300656
TI Synthesis and antitumor activity of duocarmycin derivatives: A-ring pyrrole analogs of duocarmycin B2
AU Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, 194, Japan
SO Bioorganic & Medicinal Chemistry (1996), 4(8), 1379-1391
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
GI

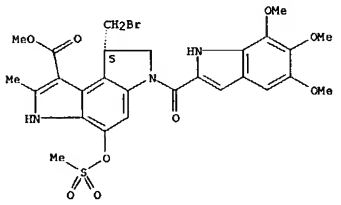


I

AB A series of the eight-substituted A-ring pyrrole derivs. of duocarmycin B2
I [R = H, Me; R1 = PhCH2O, MeO, Me2N(CH2)2O, MeSO2O, F3CSO2O, H, NC, AcO,
HCl.MeN(CH2)2N(CH2)2CO(CH2)3CO2, MeO2CO, PhO2CO, PhCH2O2CCH2NHCO2,
HO2CCH2NHCO2, L-Phe-O, PhNHCO2, 4-MeOC6H4NHCO2,
HCl.Me2CHNHCOCH2N(CH2)2N(CH2)2CO2, HCl.(CH2)5N(CH2)5NCO2, HO2CCH2N(Me)CO2,
MeN(CH2)2N(CH2)2CO2] were synthesized, and evaluated for in vitro anticellular activity against HeLa S3 cells and in vivo antitumor activity
against murine sarcoma 180 in mice. In addition, the stability of the analogs in aqueous solution was examined I (R = H, R1 = H, NC) which cannot
structurally release the cyclopropane compound (DU-86), exhibited extremely
diminished anticellular activity compared with duocarmycin A or DU-86. The ethers and the sulfonates which were not converted to DU-86 under usual conditions (35°C, pH 7), showed almost equal in vivo activities to that of duocarmycin A. However, their optimal doses were
significantly higher than that for duocarmycin A. Most of the A-ring pyrrole analogs which can be chemical or enzymically converted to DU-86,
displayed remarkably superior in vivo antitumor activity to duocarmycin A.
These results suggest that the a-ring pyrrole analogs need to chemical or
enzymically release DU-86 as an active metabolite to exhibit potent in

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
vivo antitumor activity.
IT **182360-43-6P 182360-56-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of A-ring pyrrole analogs of duocarmycin B2)
RN 182360-43-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[(methylsulfonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

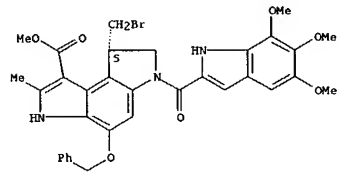


RN 182360-56-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(trifluoromethyl)sulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

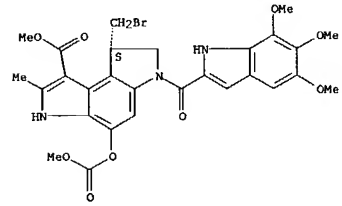
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



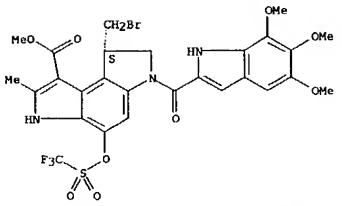
RN 182360-48-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



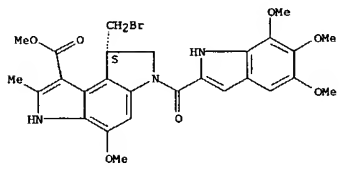
RN 182360-49-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI)

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **168776-83-8P 182360-42-5P 182360-48-1P**
182360-49-2P 182360-50-5P 182360-52-7P
182360-55-0P 182360-60-7P 182360-61-8P
182360-63-0P 182360-65-2P 182360-66-3P
182360-67-4P 182360-68-5P 182578-89-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of A-ring pyrrole analogs of duocarmycin B2)
RN 168776-83-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

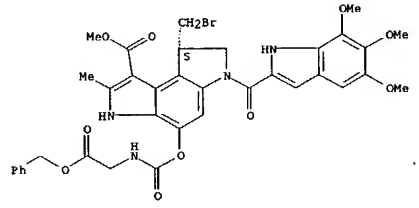
Absolute stereochemistry. Rotation (-).



RN 182360-42-5 CAPLUS

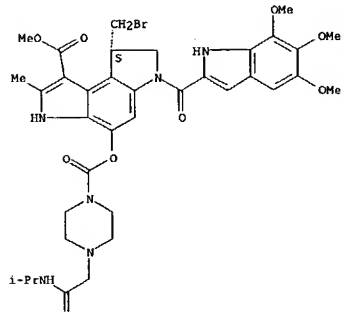
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



RN 182360-50-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-[2-[(1-methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



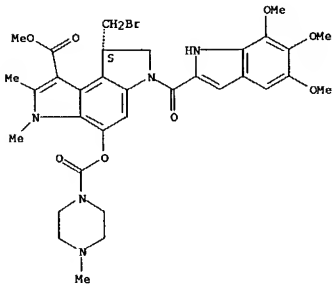
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HCl

RN 182360-52-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2,3-dimethyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)-(9CI) (CA INDEX NAME)

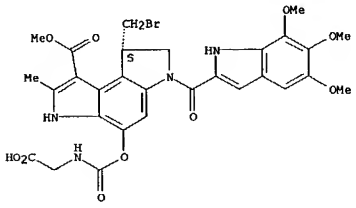
Absolute stereochemistry.



RN 182360-55-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[2-(dimethylamino)ethoxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

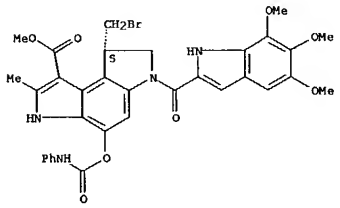
Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 182360-63-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(phenylamino)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

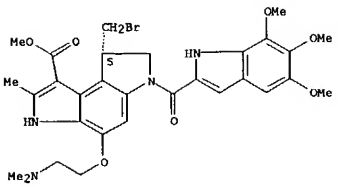
Absolute stereochemistry.



RN 182360-65-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[(4-methoxyphenyl)amino]carbonyl]oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

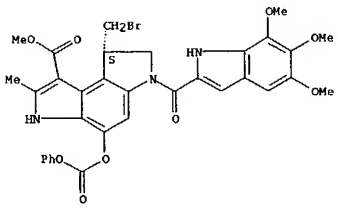
Absolute stereochemistry.

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 182360-60-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(phenoxycarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

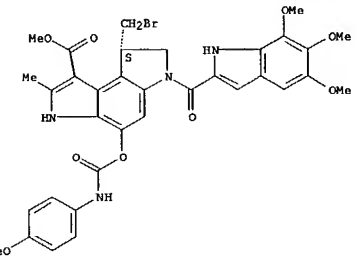
Absolute stereochemistry.



RN 182360-61-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

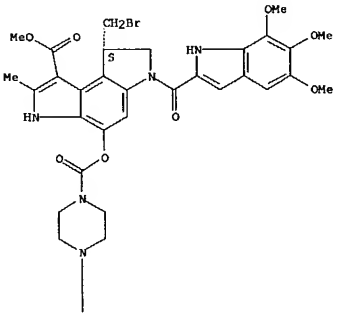
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 182360-66-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[4-(1-piperidinyl)-1-piperazinyl]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



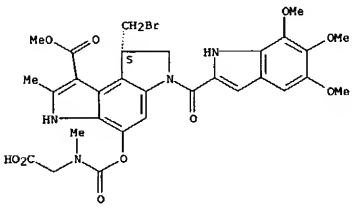
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HCl

RN 182360-67-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, (S)- (9CI)
(CA INDEX NAME)

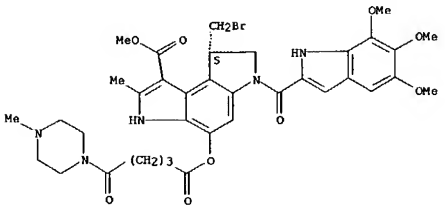
Absolute stereochemistry.



RN 182360-68-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-dioxopentyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

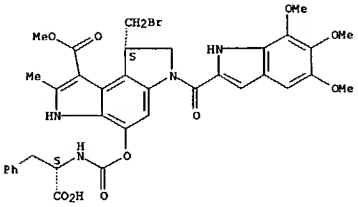
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

RN 182578-89-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1-carboxy-2-phenylethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester, [S-(R*,R*)]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

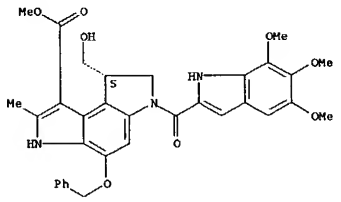


IT **182360-41-4P 182360-45-8P 182360-53-8P 182360-54-9P 182360-58-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of A-ring pyrrole analogs of duocarmycin B2)

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

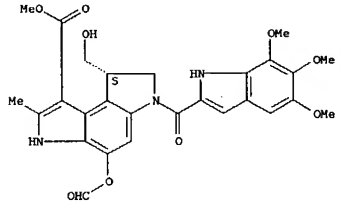
RN 182360-41-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182360-45-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(formyloxy)-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

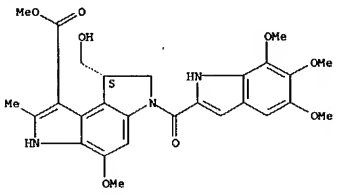


RN 182360-53-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-

L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

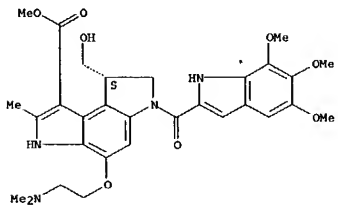
yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182360-54-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[2-(dimethylamino)ethoxy]-3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

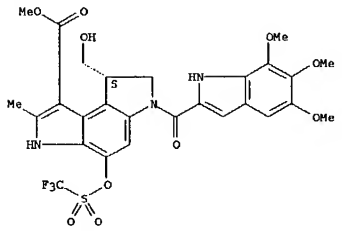
Absolute stereochemistry.



RN 182360-58-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[(trifluoromethyl)sulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

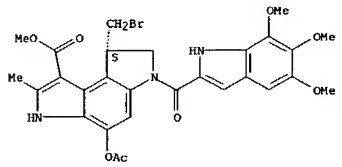
L14 ANSWER 52 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



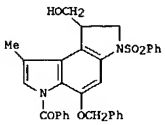
IT **182360-47-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and antitumor activity of A-ring pyrrole analogs of duocarmycin B2)
RN 182360-47-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 53 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:441562 CAPLUS
DN 125:167628
TI Enzymic preparation of optically active precursors of CPI, the DNA alkylation subunit of the naturally occurring antitumor antibiotic CC-1065
AU Ling, Lei; Lown, J. William
CS Department Chemistry, University Alberta, Edmonton, T6G 2G2, Can.
SO Chemical Communications (Cambridge) (1996), (13), 1559-1560
CODEN: CHCOFS; ISSN: 1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
GI



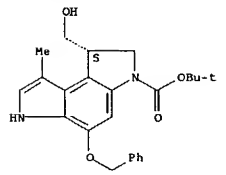
I

AB Some immediate precursors of CPI were subjected to enzymic resolution with lipase PS in vinyl acetate; racemic pyrroloindole I was effectively resolved by two consecutive enzymic reactions.

IT **112036-67-6P 180081-92-9P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(enzymic resolution of pyrroloindole precursors of CPI)
RN 112036-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) (CA INDEX NAME)

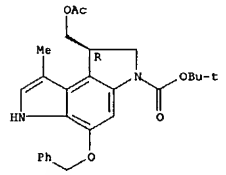
Absolute stereochemistry.

L14 ANSWER 53 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 180081-92-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI) (CA INDEX NAME)

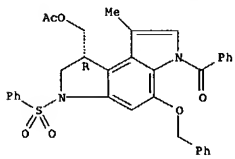
Absolute stereochemistry.



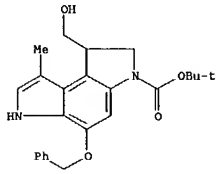
IT **180081-91-8P**
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(enzymic resolution of pyrroloindole precursors of CPI)
RN 180081-91-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 6-benzoyl-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester), (R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 53 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **112089-71-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enzymic resolution of pyrroloindole precursors of CPI)
RN 112089-71-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

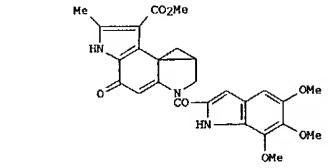


L14 ANSWER 54 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:401719 CAPLUS
DN 125:67752
TI Antitumor agent
IN Saito, Hiromitsu; Amishiro, Nobuyoshi; Nagamura, Satoru; Kobayashi, Eiji;
Okamoto, Akihiko; Gomi, Katsushige; Yamashita, Kinya; Sato, Kiyoshi; Nakakura, Masashi; Hayakawa, Eiji
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

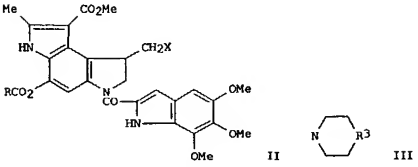
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9610405	A1	19960411	WO 1995-JP1893	19950920
	W: AU, CA, CN, FI, HU, JP, KR, NO, NZ, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2201097	AA	19960411	CA 1995-2201097	19950920
	AU 9535328	A1	19960426	AU 1995-35328	19950920
	EP 786252	A1	19970730	EP 1995-932191	19950920
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	NO 9701409	A	19970520	NO 1997-1409	19970325
	FI 9701278	A	19970527	FI 1997-1278	19970326
PRAI	JP 1994-237226		19940930		
	WO 1995-JP1893		19950920		

OS MARPAT 125:67752
GI

L14 ANSWER 54 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



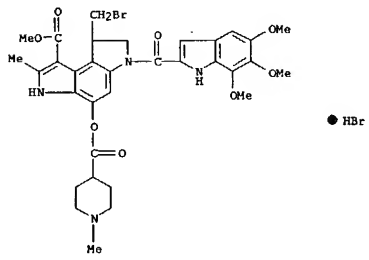
I



II III

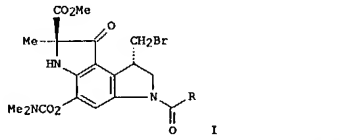
AB An antitumor agent against drug-fast tumors comprises a compound represented
by general formula (I) or (II) or a pharmacol. acceptable salt thereof as
the active ingredient; wherein X represents Cl or Br; and R represents NR1R2 (wherein R1 and R2 represent each independently hydrogen or C1-C4
linear or branched alkyl) or a group of formula (III) (wherein R3 represents CH2 or N-CH3). The agent has an excellent antitumor activity
against drug-insensitive tumors and is useful as an antitumor agent against drug-fast tumors. Capsules were formulated containing I 2, Avecel
117.5, and magnesium stearate 0.5 mg.
IT **178327-53-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor pharmaceutical compns. containing polycyclic compds. as active
ingredients)
RN 178327-53-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(1-methyl-4-piperidinyl)carbonyl]oxy]-6-[(5,6,7-

L14 ANSWER 54 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI)
(CA INDEX NAME)

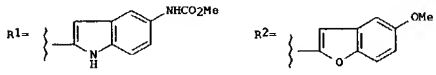


● HBr

L14 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:368752 CAPLUS
DN 125:114354
TI Synthesis and antitumor activity of novel duocarmycin derivatives
AU Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co. Ltd., Tokyo, 194, Japan
SO Bioorganic & Medicinal Chemistry Letters (1996), 6(11), 1215-1220
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
GI



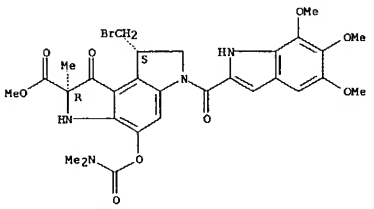
I



AB A series of Duocarmycin B2 analogs I [R = R1, R2, (E)-CH:CHC6H4OMe-4, (E)-CH:CHC6H4(NHMe)-4, CH2OC6H4OMe-4] bearing simplified right hand segments (Seg-Bs) with the protected phenolic hydroxyl group in left hand
segment (Seg-A) was synthesized. Among them, the cinnamoyl derivs. I [R =
(E)-CH:CHC6H4OMe-4, (E)-CH:CHC6H4(NHMe)-4] exhibited potent antitumor activity against in vivo murine tumor models in the wider range of doses
without detectable toxic effects than DUMB2.
IT **171599-25-0P**, Duocarmycin B2 N,N-dimethylcarbamate **179239-44-2P 179239-46-4P 179239-48-6P 179239-49-7P 179239-51-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antitumor activity of novel duocarmycin derivs.)
RN 171599-25-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-(9CI) (CA INDEX NAME)

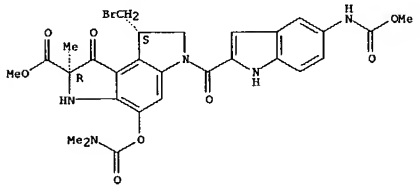
L14 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



RN 179239-44-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[[5-[(methoxycarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl
ester, (2R-trans)- (9CI) (CA INDEX NAME)

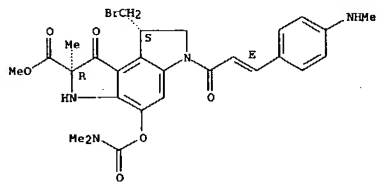
Absolute stereochemistry.



RN 179239-46-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-1-oxo-, methyl ester, (2R-trans)-
(9CI)
(CA INDEX NAME)

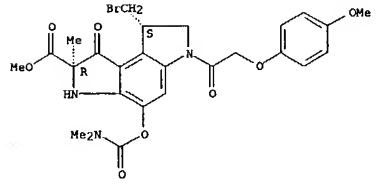
Absolute stereochemistry.

L14 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

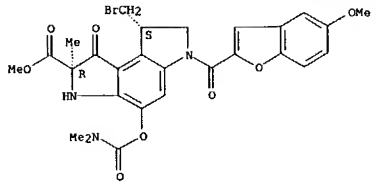


RN 179239-51-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(4-methoxyphenoxy)acetyl]-2-methyl-1-oxo-, methyl ester, (2R-trans)-
(9CI)
(CA INDEX NAME)

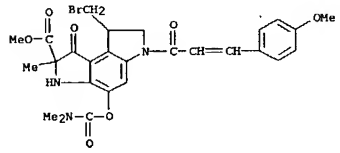
Absolute stereochemistry.



L14 ANSWER 55 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



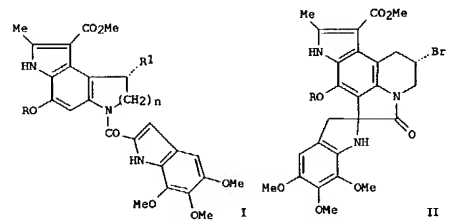
RN 179239-48-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester, [2R-[2α,6(E),8β]]- (9CI) (CA INDEX NAME)



RN 179239-49-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[3-[4-(methylamino)phenyl]-1-oxo-2-propenyl]-1-oxo-, methyl ester, [2R-[2α,6(E),8β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

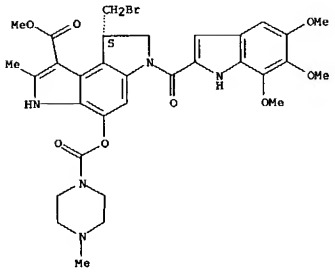
L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:325161 CAPLUS
DN 125:58167
TI Wagner-Meerwein rearrangement of duocarmycins
AU Nagamura, Satoru; Kanada, Yutaka; Asai, Akira; Kobayashi, Eiji; Gomi, Katsushige; Saito, Hiromitsu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo co., Ltd., Machida, 194,
Japan
SO Chemical & Pharmaceutical Bulletin (1996), 44(5), 933-939
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
GI



AB Treatment of 8-O-protected-3-hydroxy derivs. of duocarmycin B2 with camphorsulfonic acid (CSA) in toluene interestingly gave A-ring pyrrole
analogs I [R = SiMe2CMe3, CONMe2, 4-methylpiperazinecarbonyl (Q), R1 = CH2Br, n = 1]. Their structures were unambiguously elucidated on the basis of NMR and mass spectrometry, and the mechanism was considered to be
a Wagner-Meerwein type rearrangement. On the other hand, treatment of 9-O-protected-3-hydroxy derivs. of duocarmycin B1 with CSA afforded different rearrangement products. In the case of bulky groups at the 9-O
position, such as a tert-butyldimethylsilyl group, the normal A-ring pyrrole analog I [R= SiMe2CMe3, R1 = Br, n = 2] was obtained. Under the
same conditions, however, the 9-O-N,N-dimethylcarbamoyl-3-hydroxy compound
gave the spiro compound II [R = CONMe2], which was derived from a 1,2-shift
of the methoxycarbonyl group and a bonding between the C-8 position and
the C-2' position. The Q-protected compound gave a mixture of I [R = Q, R1 =

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Br, n = 2) and II [R = Q]. I have antitumor activity, whereas II do not.
IT **154889-68-6P 177958-19-9P 177958-20-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(Wagner-Meerwein rearrangement of duocarmycins)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

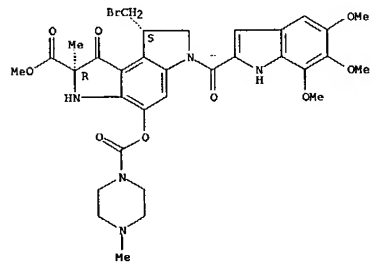


RN 177958-19-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

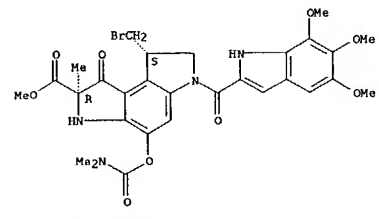
L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



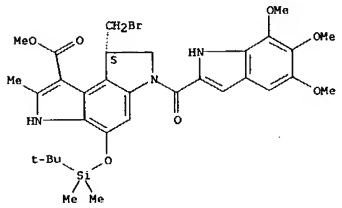
RN 171599-25-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



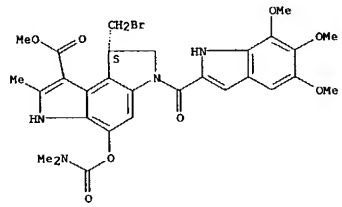
IT **129953-15-7P 129953-17-9P 160819-29-4P 177958-18-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Wagner-Meerwein rearrangement of duocarmycins)

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 177958-20-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

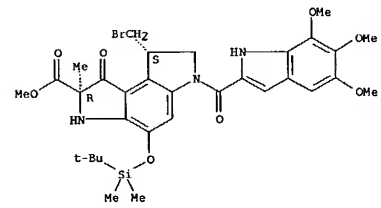
Absolute stereochemistry.



IT **154901-65-2 171599-25-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wagner-Meerwein rearrangement of duocarmycins)
RN 154901-65-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
(9CI) (CA INDEX NAME)

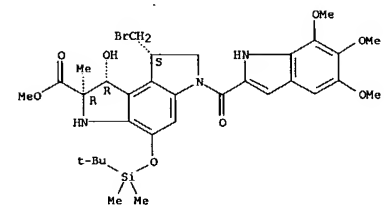
L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 129953-15-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 129953-17-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

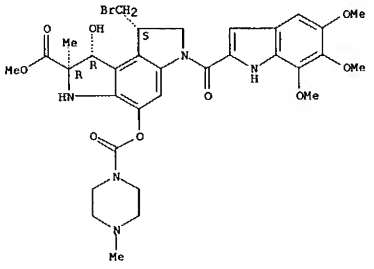


RN 160819-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[(4-methyl-1-

piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

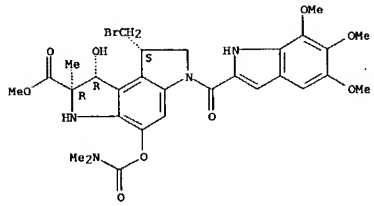
Absolute stereochemistry.



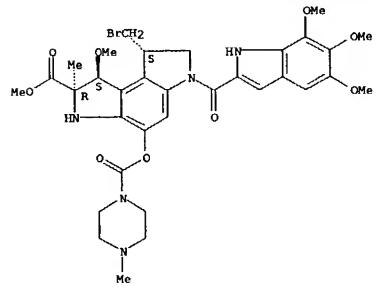
RN 177958-18-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-

[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1α,2β,8α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

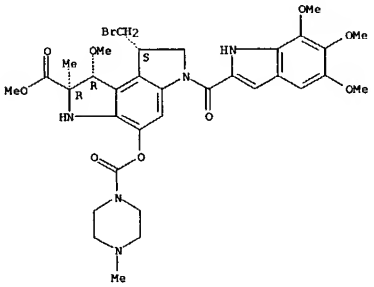


L14 ANSWER 56 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **177958-21-3P 178036-26-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(Wagner-Meerwein rearrangement of duocarmycins)
RN 177958-21-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-4-[[(4-methyl-1-

piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1α,2β,8α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 178036-26-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-methoxy-2-methyl-4-[[(4-methyl-1-

piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1S-(1α,2α,8β)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 57 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:303718 CAPLUS
DN 124:343269
TI Preparation of pyrroloindole derivatives as antitumor agents
IN Terajima, Atsuro; Fukuda, Yasumichi; Furuta, Kosuke; Oomori, Yasuo; Ko,
Hiroyuki
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 08034789	A2	19960206	JP 1994-174475	19940726
PRAI JP 1994-174475		19940726		

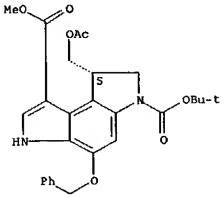
OS MARPAT 124:343269
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I and II; R = C1-4 lower alkyl; R1 = α-amino acid residue, Q, Q1, Q3, Q4, Q5, Q6, CO-W-CO; R2 = H, HO-protective group, group degradable in vivo; Y = halo, arylsulfonyloxy, lower alkanesulfonyloxy, haloalkanesulfonyloxy, N3; wherein X1, X2, X3 = H, OH, OR3, O2CR3, CHO, NO2, NR4R5, NR4COR5, NR4CO2R3, Q2, CH2NR4R5, NHCOR4R5; X4, X5, X6 = H, OR3; X7, X13 = O, S, NH; X8, X9, X10, X11, X12, X14 = CH, N; n = 0-2; wherein R3 = (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; R4, R5 = H, (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; W = (CH2)m, (CH2)m-Z4-(CH2)n, Q7; wherein m, n = 0-16; Z4 = S, O, NH], optical isomers, and pharmacol. acceptable salts, which show highly selective anticancer activity and low toxicity, are effective against solid tumors, and also have antibacterial activity, are prepared Thus, 20 mg pyrrolo[3,2-e]indole derivative I (R = Me, R1 = Boc, R2 = H, Y = Cl) (preparation given) was treated with 3 M HCl/EtOAc, stirred for 1 h, and after distilling off the solvent, stirred with 13.2 mg 5,6,7-trimethoxy-1H-indole-2-carboxylic acid and 30.2 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMF at room temperature overnight to give 79% I (R = Me, R1 = Q8, R2 = H, Y = Cl). The latter compound (10.6 mg) was suspended in MeCN, treated with 6.2 μL 1,8-diazabicyclo[5.4.0]-7-undecene, and stirred at room temperature for 5 h to

L14 ANSWER 57 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
give the title compd. cyclopropa[c]pyrrolo[3,2-e]indole (7bR,8aS)-II (R =
Me, R1 = Q8). The title compd. I (R = Me, R1 = Q9, R2 = H, Y = Cl) in
vitro showed IC50 of 0.048 ng/mL against HeLa S3 cells and at 0.25 mg/kg
in vivo inhibited by 69% the growth of colon 26 cancer cells in mice.
IT **176685-39-5P 176685-40-8P 176685-41-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of pyrrolobenzocarbazoledione and cyclopropapyrrolobenzocarbazo
letrione derivs. as antitumor agents)
RN 176685-39-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

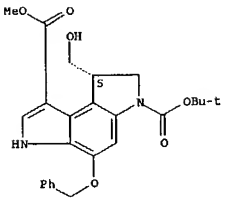
Absolute stereochemistry. Rotation (-).



RN 176685-40-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

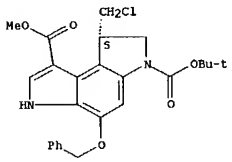
Absolute stereochemistry. Rotation (-).

L14 ANSWER 57 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 176685-41-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L14 ANSWER 58 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:301099 CAPLUS
DN 124:343266
TI Preparation of (trifluoromethyl)pyrroloindole and -cyclopropapyrroloindole derivatives as antitumor agents
IN Terajima, Atsuro; Fukuda, Yasumichi; Oomori, Yasuo
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
SO Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

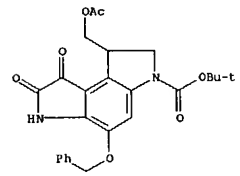
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08034786	A2	19960206	JP 1994-174472	19940726
PRAI	JP 1994-174472		19940726		

OS MARPAT 124:343266
GI

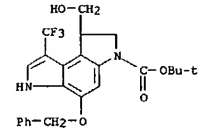
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I and II; R1 = α-amino acid residue, Q, Q1, Q3, Q4, Q5, Q6, CO-W-CO; R2 = H, HO-protective group, group degradable in vivo; Y = halo, arylsulfonyloxy, lower alkanesulfonyloxy, haloalkanesulfonyloxy, N3; wherein X1, X2, X3 = H, OH, OR3, O2CR3, CHO, NO2, NR4R5, NR4COR5, NR4CO2R3, Q2, CH2NR4R5, NHCOR4R5; X4, X5, X6 = H, OR3; X7, X13 = O, S, NH; X8, X9, X10, X11, X12, X14 = CH, N; n = 0-2; wherein R3 = (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; R4, R5 = H, (un)substituted linear or branched C1-6 alkyl, (un)substituted aryl; W = (CH2)m, (CH2)m-Z4-(CH2)n, Q7; wherein m, n = 0-16; Z4 = S, O, NH], optically active isomers, and pharmacol. acceptable salts, which show highly selective anticancer activity and low toxicity, are effective against solid tumors, and also have antibacterial activity, are prepared Thus, 11.3 mg pyrrolo[3,2-e]indole derivative I (R1 = Boc, R2 = PhCH2, Y = Cl) (preparation given) was dissolved in CH2Cl2, treated dropwise with a solution of BBr3 in CH2Cl2 (70.5 μL, 0.0705 mmol), allowed to react for 1.75 h, centrifuged to remove the supernatant liquid, dried, treated with 7.5 mg 5-(benzofuran-2-carbonyl)amino-1H-indole-2-carboxylic acid and 13.5 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and stirred in DMF for 4.5 h to give 42% I (R1 = Q8). The latter compound in vitro showed IC50 of 0.49 ng/mL against P388 cells and at

L14 ANSWER 58 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
0.5 mg/kg in vivo inhibited by 86% the growth of colon 26 cancer cells in mice.
IT **132628-62-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (trifluoromethyl)pyrroloindole and -cyclopropapyrroloindole derivs. as antitumor agents)
RN 132628-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

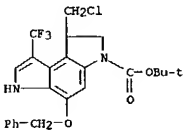


IT **176539-79-0P 176539-80-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of (trifluoromethyl)pyrroloindole and -cyclopropapyrroloindole derivs. as antitumor agents)
RN 176539-79-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-8-(trifluoromethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 176539-80-3 CAPLUS

L14 ANSWER 58 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-5-(phenylmethoxy)-8-(trifluoromethyl)-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)



L14 ANSWER 59 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:248963 CAPLUS
DN 125:11480
TI Cyclopropapyrroloindole-oligopeptide anticancer agents
IN Lown, J. William; Wang, Yuqiang; Luo, Weide
PA Synphar Laboratories, Inc., Can.
SO U.S., 17 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

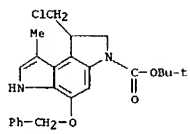
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5502068	A	19960326	US 1995-381355	19950131
	CA 2210093	AA	19960808	CA 1996-2210093	19960131
	WO 9623497	A1	19960808	WO 1996-US727	19960131
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	AU 9649643	A1	19960821	AU 1996-49643	19960131
	AU 698001	B2	19981022		
	EP 800390	A1	19971015	EP 1996-906176	19960131
	EP 800390	B1	20021204		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 11500427	T2	19990112	JP 1996-523576	19960131
	AT 228837	E	20021215	AT 1996-906176	19960131
PRAI	US 1995-381355	A	19950131		
	WO 1996-US727	W	19960131		

OS MARPAT 125:11480
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is directed to novel cyclopropylpyrroloindole-oligopeptide
compds. which are useful as anticancer agents. The novel
cyclopropylpyrroloindole-oligopeptide compds. have the following general
structure: I wherein, Het1 and Het2 are individually selected from the
group consisting of pyrrole, imidazole, N-alkylimidazole,
N-alkoxymethylimidazole, thiophene, thiophene, furan, thiazole, oxazole,

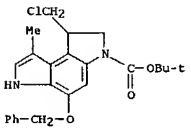
L14 ANSWER 59 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
N-alkylpyrrole, N-alkoxymethylpyrrole and pyrazole, R is selected from the
group consisting of a valence bond; a divalent C1-C6 alkyl; a divalent
C2-C6 alkenyl; a divalent C2-C6 alkynyl; a divalent cycloalkane of formula
CpH2p-2 wherein p is 3 to 7; and an ortho, meta or para linked arom.
group, A is selected from the group consisting of a C1-C6 alkyl group; an
amidine or deriv. thereof; a guanidine; a secondary, tertiary or
quaternary ammonium salt; and a sulfonium salt, n is 0 to 3, and m is 0 to
3, wherein when n=0, m is 1-3. Thus, e.g., deprotection of
5-benzyloxy-3-tert-butyloxycarbonyl-1-chloromethyl-8-methyl-1,2-dihydro-3H-
pyrrolo[3,2-e]indole (II) followed by coupling with 4-(4-butyramido-N-
methyl-2-pyrrolecarboxyamido)-N-methyl-2-pyrroleacrylic acid and ring
closure afforded
(E)-1,2,8,8a-tetrahydro-7-methyl-2-[4-(4-butyramido-N-
methyl-2-pyrrolecarboxyamido)-N-methyl-2-pyrroleacryloyl]cyclopropa[c]pyrr
olo[3,2-e]indole-4-(5H)-one [(E)-III] which exhibited cytotoxicity of TD50
= 9.50 + 10-10 μg/mL for KB human nasopharyngeal tumor cells
(TD50 = 1 + 10-6 μg/mL for CC-1065). A detailed anal. of the
frequency of occurrence of bases flanking the prominent DNA alkylation
sites for III is given and compared with CC-1065, providing evidence of
the main cellular event that gives rise to the expression of anticancer
properties of the new drugs and how they differ in detail from CC-1065.
IT **175614-07-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclopropapyrroloindole-oligopeptide anticancer agents)
RN 175614-07-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA
INDEX NAME)



L14 ANSWER 59 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L14 ANSWER 60 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:185423 CAPLUS
DN 124:278276
TI Design, synthesis, cytotoxic properties and preliminary DNA sequencing
evaluation of CPI-N-methylpyrrole hybrids. Enhancing effect of a trans
double bond linker and role of the terminal amide functionality on cytotoxic potency
AU Wang, Yuqiang; Gupta, Rajan; Huang, Liren; Luo, Weide; Lown, J. William
CS Dep. of Chemistry, Univ. of Alberta, Edmonton, AB, T6G 2G2, Can.
SO Anti-Cancer Drug Design (1996), 11(1), 15-34
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
AB In an approach to the design and exploration of the properties of cyclopropylindole (CPI)-lexitropsin conjugates as potential anticancer
agents, CPI-N-methylpyrroles of two sep. classes have been synthesized and
characterized. These comprise structures (i) in which the N-methylpyrrole
moiety bears amide groups of different sizes and (ii) in which both flexible and rigid linkers are introduced between the CPI and
N-methylpyrrole units. The extent and the relative rates of DNA cleavage
following alkylation and thermal treatment by these CPI conjugates were
determined by an agarose gel mobility shift assay. The DNA sequence
preferences of the 7 new agents were also determined in a preliminary study by
high-resolution polyacrylamide gel electrophoresis and contrasted with that
of CC-1065. The CPI-N-methylpyrrole agents avoid the major alkylation
sites of CC-1065, but all alkylate the minor CC-1065 site of 5'AATA and
exhibit a consensus sequence of 5'-N.A/T.A/T.A. The cytotoxicities of
these compds. were determined against KB human tumor cells in vitro. Compound 6,
bearing a 4-butyramide group in the N-methylpyrrole, is 100 times more
potent than 7 which lacks an amide group, while 10 which bears a rigid
trans double bond linker is 100 times more potent than its flexible ethyl-linked counterpart.
IT **175614-07-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(design, synthesis, cytotoxic properties and preliminary DNA sequencing

L14 ANSWER 60 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
evaluation of cyclopropylindole-N-methylpyrrole hybrids)
RN 175614-07-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA
INDEX NAME)

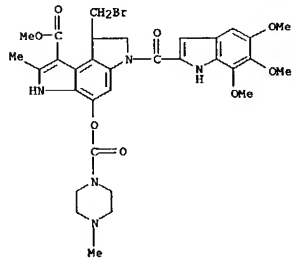


L14 ANSWER 61 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:115202 CAPLUS
DN 124:156002
TI Method for stabilizing duocarmycin derivatives
IN Nakakura, Masashi; Ueno, Yuji; Hayakawa, Eiji; Kuroda, Tokuyuki
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9531971	A1	19951130	WO 1995-JP962	19950519
W: AU, BR, CA, CN, CZ, FI, HU, KR, MX, NO, NZ, PL, RO, RU, SI, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 07309761	A2	19951128	JP 1994-106415	19940520
CA 2190635	AA	19951130	CA 1995-2190635	19950519
AU 9524551	A1	19951218	AU 1995-24551	19950519
EP 754030	A1	19970122	EP 1995-918749	19950519
EP 754030	B1	20001220		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1148805	A	19970430	CN 1995-193164	19950519
BR 9507640	A	19970819	BR 1995-7640	19950519
HU 78072	A2	19990830	HU 1996-3521	19950519
AT 198149	E	20010115	AT 1995-918749	19950519
US 5703080	A	19971230	US 1996-737145	19961030
NO 9604813	A	19961113	NO 1996-4813	19961113
FI 9604624	A	19961119	FI 1996-4624	19961119
PRAI JP 1994-106415	A	19940520		
WO 1995-JP962	W	19950519		

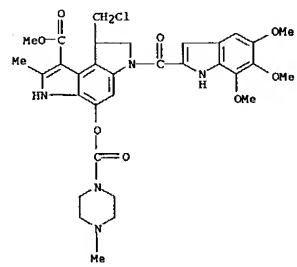
OS MARPAT 124:156002
AB Stabilized duocarmycin derivs. are prepared by adding at least a compound
selected from the group consisting of saccharides, electrolytes, water-soluble polymers, polyhydric alcs. and surfactants to a solution containing
the duocarmycin derivs. Also provided are freeze-dried pharmaceutical
preprns. containing the stabilized duocarmycin derivs. Citric acid 50,
duocarmycin·HBr (I) 100, and lactose 5000 mg were dissolved in distilled water to make a total volume of 200 mL. The resulting solution was
placed into vials in 2 mL portions, and freeze-dried under reduced pressure. After storage at 60° for 30 days, HPLC anal. showed that 100% of I remained.
IT **134106-78-8 134106-81-3 173552-35-7**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(freeze-dried preprns. containing stabilized duocarmycin derivs.)
RN 134106-78-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134106-81-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

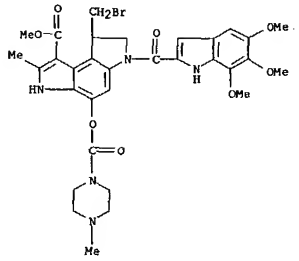


RN 173552-35-7 CAPLUS

L14 ANSWER 61 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



● HBr

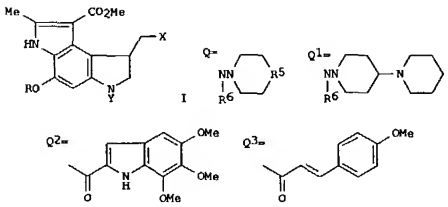
PAGE 2-A

● H_2O

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:998395 CAPLUS
DN 124:176153
TI Preparation of DC-89 derivatives as antitumor agents
IN Amishiro, Nobuyoshi; Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji; Okamoto, Akihiko; Gomi, Katsushige
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9529179	A1	19951102	WO 1995-JP779	19950420
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2165819	AA	19951102	CA 1995-2165819	19950420
	AU 9522671	A1	19951116	AU 1995-22671	19950420
	AU 685939	B2	19980129		
	EP 705833	A1	19960410	EP 1995-916020	19950420
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5641780	A	19970624	US 1995-564178	19951215
PRAI	JP 1994-84714	A	19940422		
	WO 1995-JP779	W	19950420		

OS MARPAT 124:176153
GI



AB DC-89 derivs. [I; X = Cl or Br; R = (un)substituted alkyl, (un)substituted

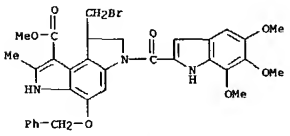
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
aralkyl, COR1, OR2, SR2, NR3R4, Q, Q1, SO2R8; wherein R1 = H, (un)substituted alkyl, aryl, or heterocyclyl; R2 = (un)substituted alkyl, aryl; R3, R4 = H, (un)substituted alkyl, NH2, mono- or dialkylamino; provided that R3 = R4 ≠ H; R5 = NR7, O ; R6, R7 = H, (un)substituted alkyl; R8 = (un)substituted alkyl or aryl; Y = Q2, Q3] or pharmacol. acceptable salts thereof are prepd. Thus, the tert-butyldimethylsilyl ether I (R = Me3CSiMe2, X = Br, Y = Q2) (50 mg) was dissolved in THF, treated with 0.11 mL 1.0 M Bu4NF/THF, and stirred at room temp. for 1 h to give, after workup, the alc. I (R = H, X = Br, Y = Q2) which was dissolved in MeCN, treated with 48% aq. HBr, stirred at room temp. for 1 h, treated with 1 N aq. HBr, and extd. with CHCl3. The CHCl3 ext. was dried over anhyd. Na2SO4 and evapd. to dryness to give the crude product which was dissolved in CH2Cl2, treated with 0.027 mL Ph chloroformate and 0.030 mL Et3N, and stirred at -78° to 0° for 1 h to give, after workup and silica gel chromatog., the title pyrroloindoline I (R = CO2Ph, X = Br, Y = Q2). The latter compd. in vitro showed IC50 of 0.051 nM for inhibiting the proliferation of HeLaS3 cells and in vivo exhibited T/C of 0.090 (tumor vol. of the treated animal/tumor vol. of the control) in mice transplanted with sarcoma 180.

IT **173903-48-5P 173903-49-6P 173903-50-9P**
173903-51-0P 173903-52-1P 173903-53-2P
173903-54-3P 173903-55-4P 173903-56-5P
173903-57-6P 173903-58-7P 173903-59-8P
173903-60-1P 173903-61-2P 173903-62-3P
173903-63-4P 173903-64-5P 173903-65-6P
173903-66-7P 173903-67-8P 173903-68-9P
173903-69-0P 173903-70-3P 173903-71-4P
173903-72-5P 173903-73-6P 173903-74-7P
173903-75-8P 173903-76-9P 173903-77-0P
173903-78-1P 173903-79-2P 173903-80-5P
173903-81-6P 173903-82-7P 173903-83-8P
173903-84-9P 173903-85-0P 173903-86-1P
173903-87-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); *BIOL (Biological study); PREP (Preparation); USES (Uses)*
(preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)

RN 173903-48-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

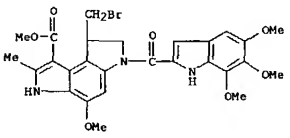
tetrahydro-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



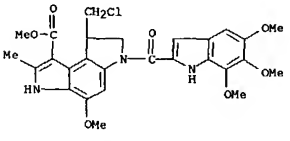
RN 173903-49-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-50-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

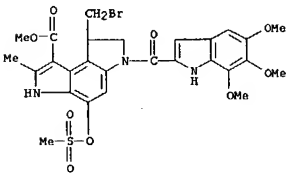
tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



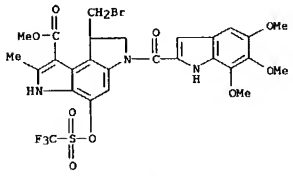
RN 173903-51-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

tetrahydro-2-methyl-4-[(methylsulfonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

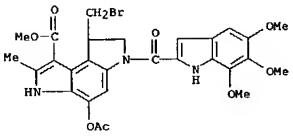


RN 173903-52-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(trifluoromethyl)sulfonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

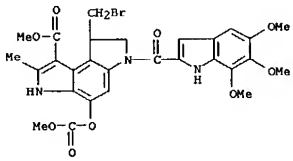


RN 173903-53-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

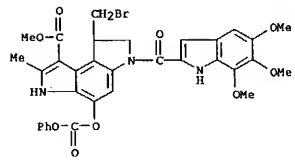


RN 173903-54-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

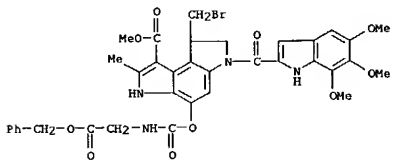


RN 173903-55-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[(phenoxycarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

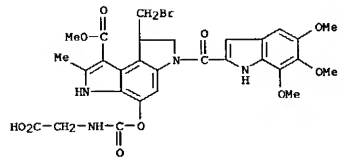


RN 173903-56-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[[[2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

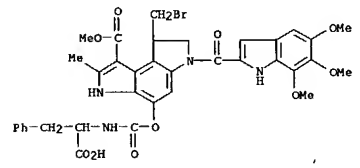


RN 173903-57-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)

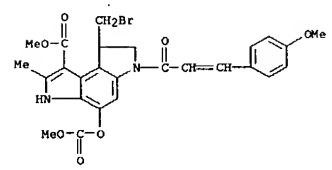
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



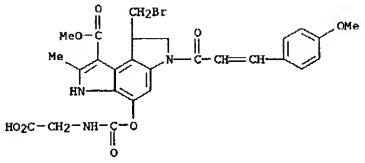
RN 173903-58-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(1-carboxy-2-phenylethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)



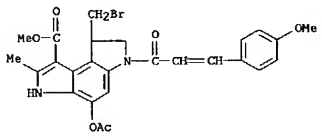
RN 173903-59-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 173903-60-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester (9CI) (CA INDEX NAME)

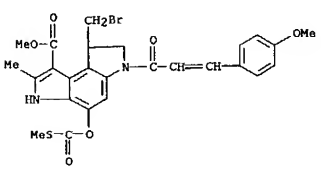


RN 173903-61-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

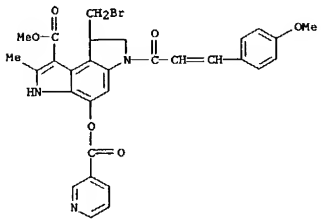


RN 173903-62-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(methylthio)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

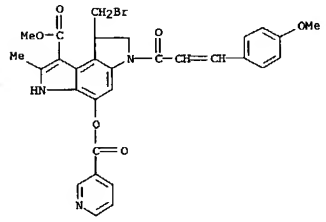


RN 173903-63-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



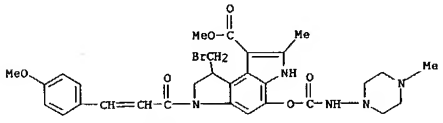
RN 173903-64-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



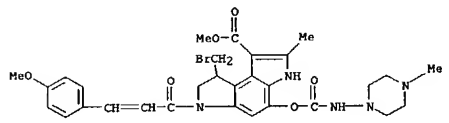
● HCl

RN 173903-65-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



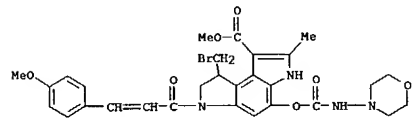
RN 173903-66-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



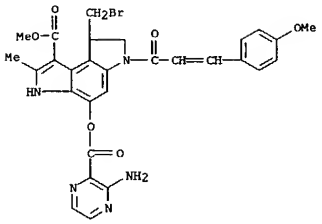
● HCl

RN 173903-67-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-morpholinylamino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



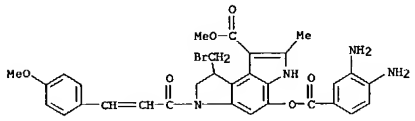
RN 173903-68-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[(3-aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173903-69-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[(3,4-

diaminobenzoyl)oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



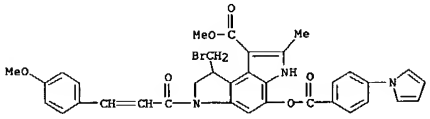
RN 173903-70-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-

(dimethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173903-73-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

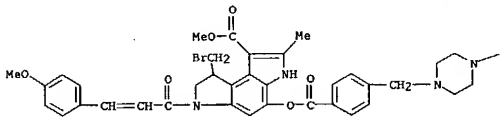
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-(1H-pyrrol-1-yl)benzoyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-74-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

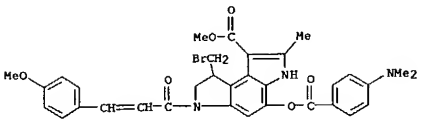


PAGE 1-B

RN 173903-75-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

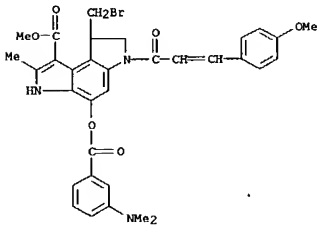
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, monohydrobromide

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



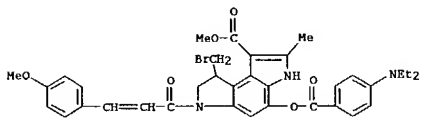
RN 173903-71-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[3-

(dimethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



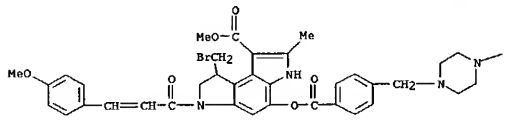
RN 173903-72-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-

(diethylamino)benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

PAGE 1-A

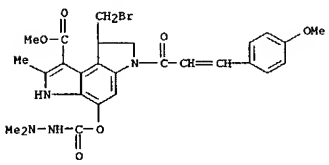


● HBr

PAGE 1-B

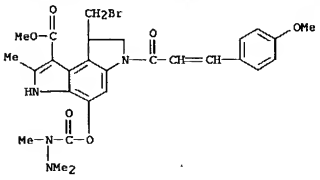
RN 173903-76-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(2,2-

dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

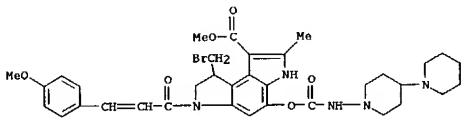


RN 173903-77-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(trimethylhydrazino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

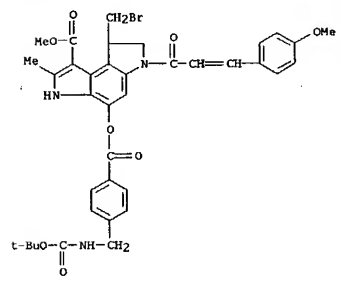


RN 173903-78-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[1,4'-bipiperidin]-1'-ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

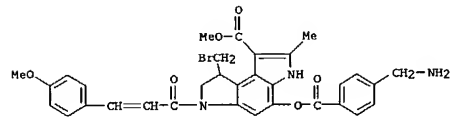


RN 173903-79-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[[1,4'-bipiperidin]-1'-ylamino)carbonyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

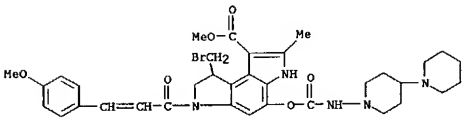


RN 173903-82-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



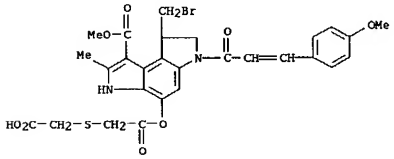
RN 173903-83-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[4-(aminomethyl)benzoyl]oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



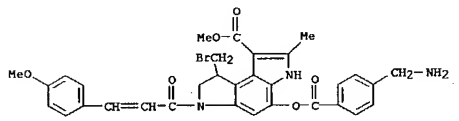
● HBr

RN 173903-80-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester (9CI) (CA INDEX NAME)



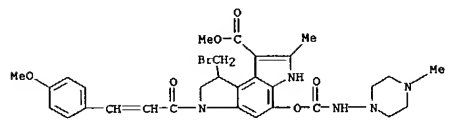
RN 173903-81-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]benzoyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HBr

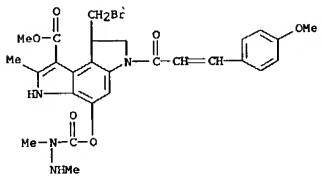
RN 173903-84-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)



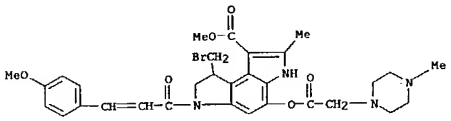
● HBr

RN 173903-85-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



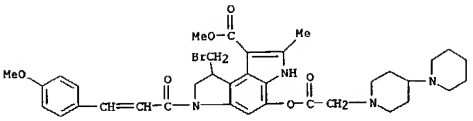
RN 173903-86-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)acetyl]oxy]-, methyl ester, dihydrobromide (9CI) (CA INDEX NAME)



●2 HBr

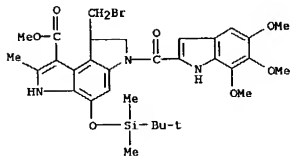
RN 173903-87-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[([1,4'-bipiperidin]-1'-ylacetyl)oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, dihydrobromide (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



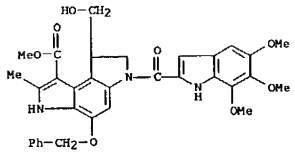
●2 HBr

IT 134127-18-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)
RN 134127-18-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

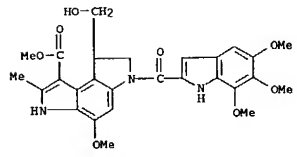


IT 173903-89-4P 173903-90-7P 173903-91-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of DC-89 (pyrroloindoline) derivs. as antitumor agents)
RN 173903-89-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

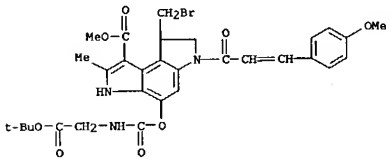


RN 173903-90-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 173903-91-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[2-(1,1-dimethylethoxy)-2-oxoethyl]amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)

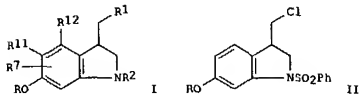
L14 ANSWER 62 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 63 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:997014 CAPLUS
DN 124:145899
TI Preparation of 6-hydroxyindoline acetals and analogs as cytostatic prodrugs
IN Tietze, Lutz F.
PA Germany
SO Ger. Offen., 39 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

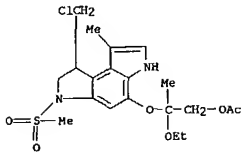
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4415463	A1	19951109	DE 1994-4415463	19940503
	DE 4415463	C2	19960926		
PRAI	DE 1994-4415463		19940503		

OS MARPAT 124:145899
GI



AB Title compds. [I; R = CR4(OR3)CHR5R6, R8; R1 = halo, alkylsulfonyloxy, OSO2Ph, etc.; R2 = (un)substituted alkyl, alkylsulfonyloxy, Ac, alkoxycarbonyl, etc.; R3 = (un)substituted alkyl, hydroxy-protective group, sugar residue; R4-R7 = H, (un)substituted alkyl; R8 = sugar residue; R11,R12 = H; R11R12 = NR10CH:CR9; R9,R10 = H, alkyl] were prepared
Thus, hydroxyindoline II (R = H) (preparation given) was condensed with CH2:CHOEt to give *II* (R = CHMeOEt) which gave pH 6.2 growth of bronchial carcinoma cells A 549 47.14% of control at 3.0μg/mL in vitro.
IT **173368-66-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6-hydroxyindoline acetals and analogs as cytostatic prodrugs)
RN 173368-66-6 CAPLUS

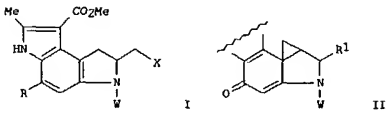
L14 ANSWER 63 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole, 5-[2-(acetyloxy)-1-ethoxy-1-methylethoxy]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:996496 CAPLUS
DN 124:116964
TI Preparation of DC-89 derivatives as antitumors
IN Amishiro, Nobuyoshi; Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji; Okamoto, Akihiko; Gomi, Katsushige
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9526964	A1	19951012	WO 1995-JP626	19950331
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9520848	A1	19951023	AU 1995-20848	19950331
	AU 689566	B2	19980402		
	EP 702014	A1	19960320	EP 1995-913398	19950331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5670492	A	19970923	US 1995-557055	19951128
PRAI	JP 1994-65236		19940401		
	WO 1995-JP626		19950331		

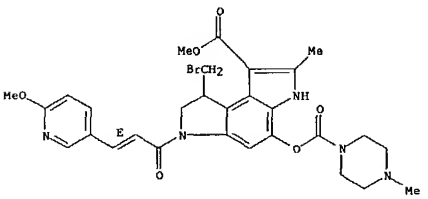
OS MARPAT 124:116964
GI



AB DC-89 derivs. e.g. I [W = heterocyclylalkenoyl, acylalkenoyl, etc.; X = Cl, Br; R = acyloxy, 4-alkylpiperazin-1-ylamino] and II (R1 = H, CH2-X; X and W same as above) and their pharmaceutically acceptable salts, having excellent antitumor activity and useful as antitumor drugs, are prepared
Thus, *a mixture of II [W = R1 = H] was reacted with p-nitrophenyl* (E)-3-(6-methoxy-3-pyridinyl)acrylate in DMF containing NaH at -20° for 2 h to give 78% II [W = (E)-3-(6-methoxy-3-pyridinyl)acryloyl, R1 = H].
This at 1.0 mg/Kg i.v. had an IC50 of 0.42 nM against sarcoma 180 tumors in mice.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **173087-75-7P 173087-76-8P 173087-78-0P**
173087-80-4P 173087-82-6P 173087-84-8P
173087-86-0P 173087-90-6P 173087-93-9P
173087-95-1P 173087-96-2P 173087-98-4P
173087-99-5P 173088-00-1P 173088-01-2P
173088-02-3P 173088-03-4P 173088-04-5P
173088-05-6P 173088-06-7P 173088-07-8P
173088-08-9P 173088-09-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of duocarmycin B1 derivs. as antitumors)
RN 173087-75-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

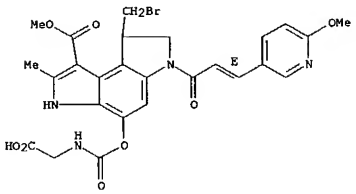
Double bond geometry as shown.



RN 173087-76-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI) (CA INDEX NAME)

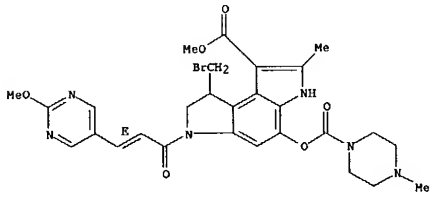
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



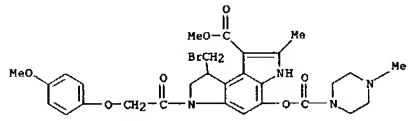
RN 173087-78-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

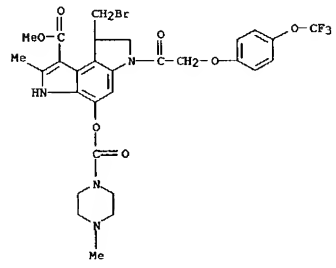


RN 173087-80-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173087-86-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[4-(trifluoromethoxy)phenoxy]acetyl]-, methyl ester (9CI) (CA INDEX NAME)

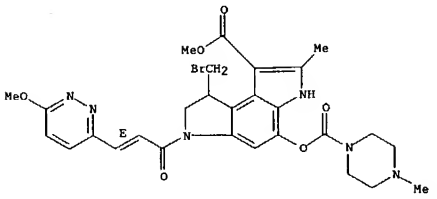


RN 173087-90-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

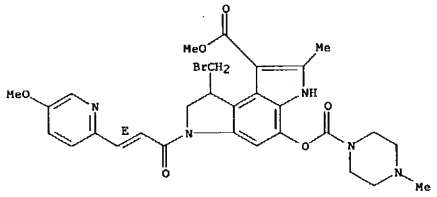
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Double bond geometry as shown.



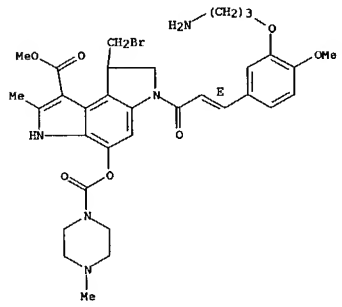
RN 173087-82-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



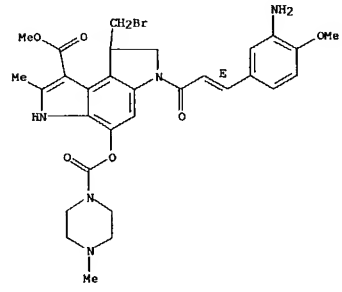
RN 173087-84-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(4-methoxyphenoxy)acetyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173087-93-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

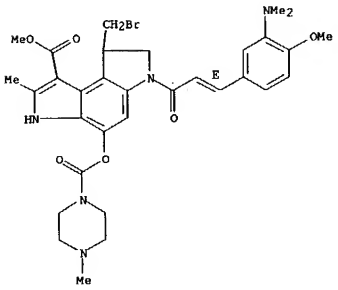


RN 173087-95-1 CAPLUS

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

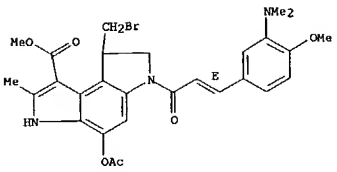


RN 173087-96-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-
3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX
NAME)

Double bond geometry as shown.

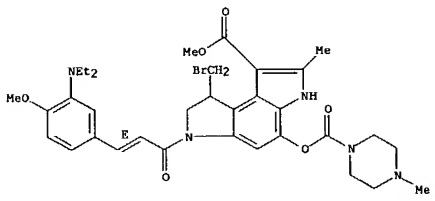
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173087-98-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

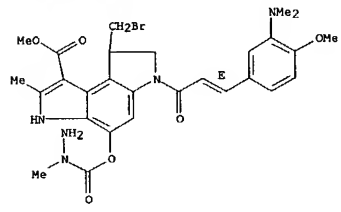


RN 173087-99-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, (E)- (9CI)
(CA INDEX NAME)

Double bond geometry as shown.

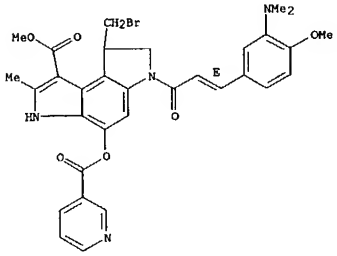
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-00-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA
INDEX
NAME)

Double bond geometry as shown.

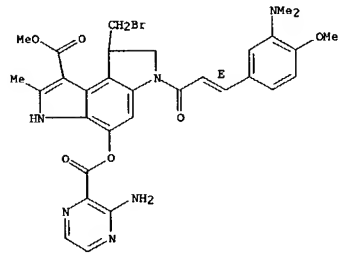


RN 173088-01-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[(3-

aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-
methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl
ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

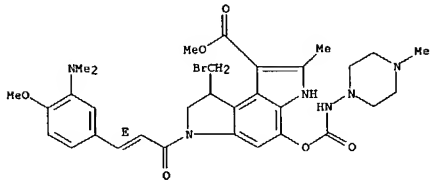
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-02-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl
ester,
(E)- (9CI) (CA INDEX NAME)

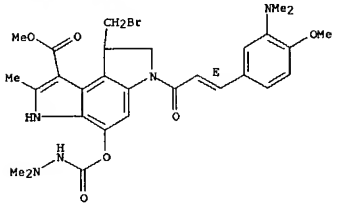
Double bond geometry as shown.



RN 173088-03-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-
(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(2,2-
dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl
ester, (E)- (9CI) (CA INDEX NAME)

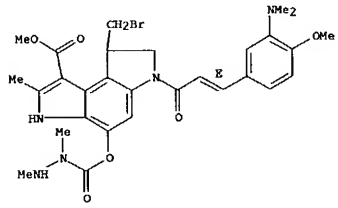
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-04-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-
(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(1,2-
dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl
ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

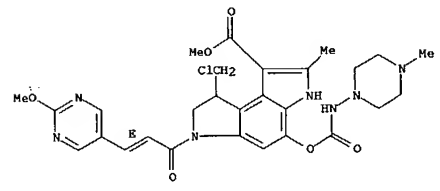


RN 173088-05-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl
ester,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

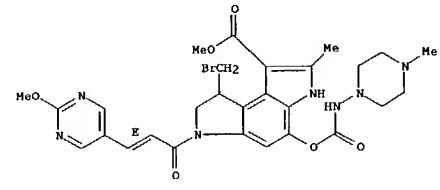
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-07-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-
[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (E)-
(9CI)
(CA INDEX NAME)

Double bond geometry as shown.



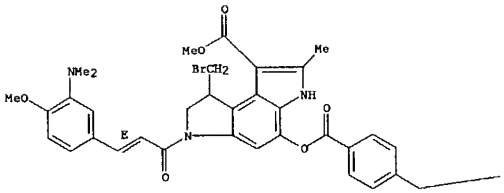
RN 173088-08-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4
-
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, (E)-
(9CI)
(CA INDEX NAME)

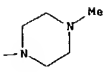
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



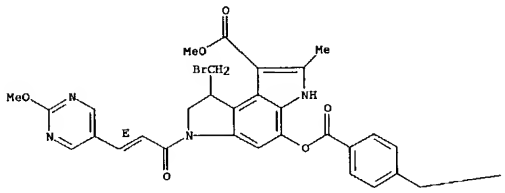
RN 173088-06-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-
[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, (E)-
(9CI)
(CA INDEX NAME)

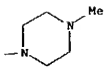
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

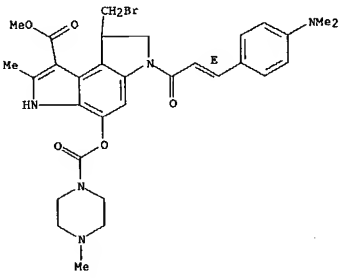


RN 173088-09-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[4-

(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-
[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, (E)- (9CI)
(CA
INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



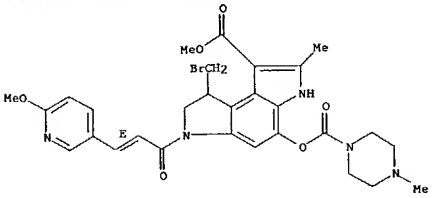
IT 173088-10-3P 173088-11-4P 173088-12-5P
173088-13-6P 173088-14-7P 173088-15-8P
173088-16-9P 173088-17-0P 173088-18-1P
173088-21-6P 173088-24-9P 173088-27-2P
173088-28-3P 173088-29-4P 173088-30-7P
173088-31-8P 173088-32-9P 173088-33-0P
173088-34-1P 173088-35-2P 173088-36-3P
173088-37-4P 173088-38-5P 173088-39-6P
173088-40-9P 173088-41-0P 173088-42-1P
173088-43-2P 173088-44-3P 173088-45-4P
173088-46-5P 173088-47-6P 173088-48-7P
173088-49-8P 173088-50-1P 173088-51-2P
173088-52-3P 173088-55-6P 173088-56-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of duocarmycin B1 derivs. as antitumors)

RN 173088-10-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride, (E)-
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

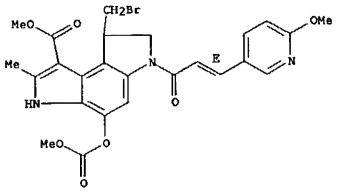


● HCl

RN 173088-11-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(6-methoxy-3-pyridinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

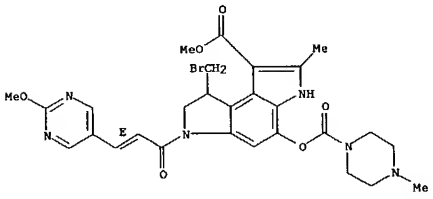


RN 173088-12-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride,

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

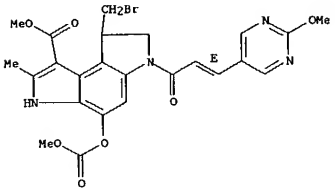


● HCl

RN 173088-13-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[(methoxycarbonyl)oxy]-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

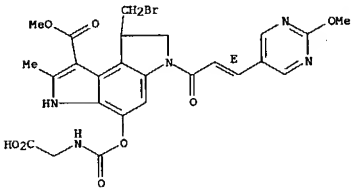


RN 173088-14-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[[(carboxymethyl)amino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI)
(CA

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

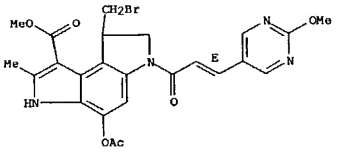
Double bond geometry as shown.



RN 173088-15-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-

(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

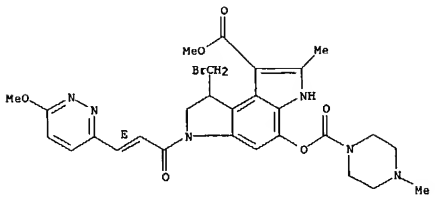


RN 173088-16-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(6-methoxy-3-pyridazinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrochloride,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

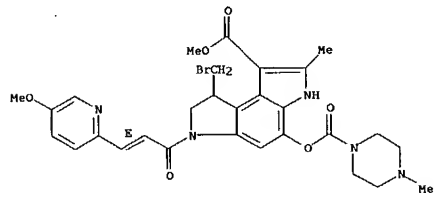
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

RN 173088-17-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(5-methoxy-2-pyridinyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

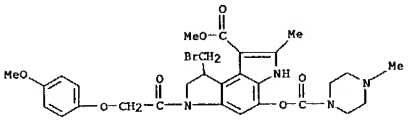
Double bond geometry as shown.



● HCl

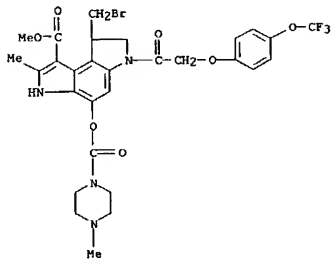
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173088-18-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[(4-methoxyphenoxy)acetyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 173088-21-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[4-(trifluoromethoxy)phenoxy]acetyl]-, methyl ester, monohydrochloride (9CI)
(CA INDEX NAME)



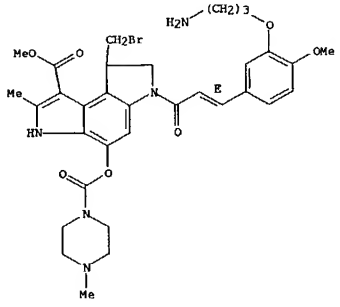
● HCl

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173088-24-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-[3-(3-aminopropoxy)-4-methoxyphenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



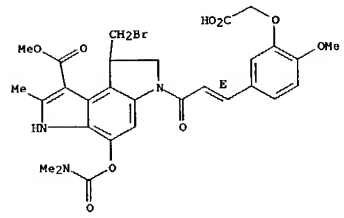
PAGE 2-A

●2 HCl

RN 173088-27-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(carboxymethyl)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, 1-methyl ester, (E)- (9CI) (CA INDEX NAME)

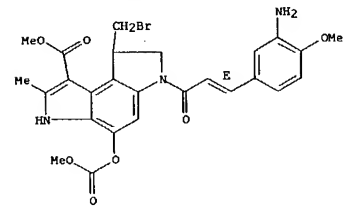
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

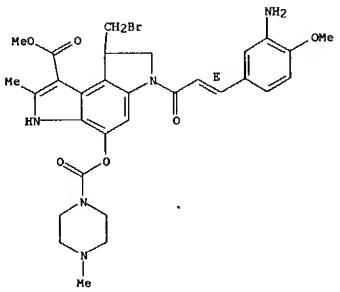


RN 173088-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

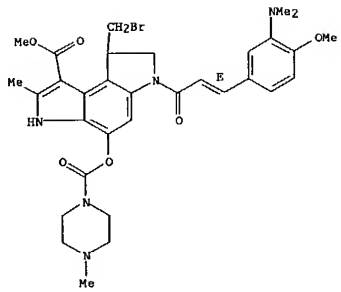
●2 HCl

RN 173088-30-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



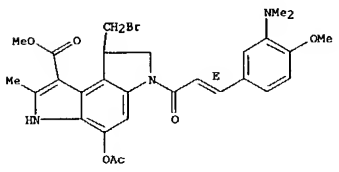
PAGE 2-A

●2 HCl

RN 173088-31-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

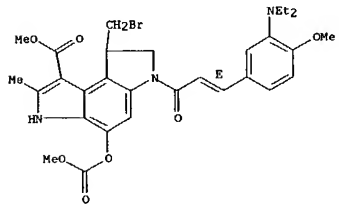
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

RN 173088-32-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-4-[(methoxycarbonyl)oxy]-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

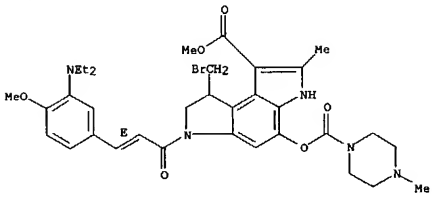
Double bond geometry as shown.



RN 173088-33-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(diethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, dihydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

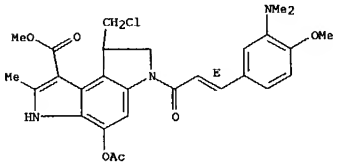
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



●2 HCl

RN 173088-34-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA INDEX NAME)

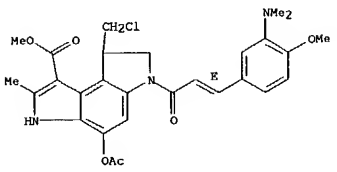
Double bond geometry as shown.



RN 173088-35-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrochloride, (E)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

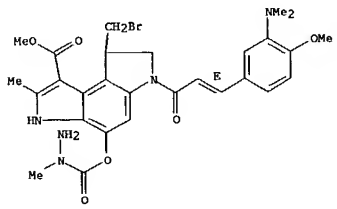
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HCl

RN 173088-36-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(1-methylhydrazino)carbonyl]oxy]-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



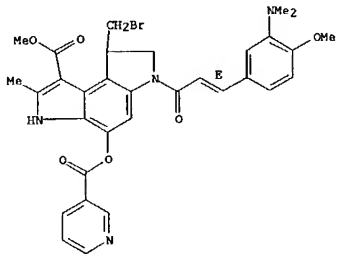
● HBr

RN 173088-37-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(3-pyridinylcarbonyl)oxy]-, methyl ester, dihydrobromide, (E)-
(9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Double bond geometry as shown.

PAGE 1-A



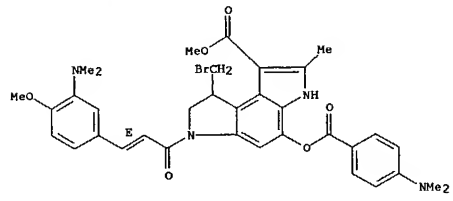
PAGE 2-A

●2 HBr

RN 173088-38-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[4-(dimethylamino)benzoyl]oxy]-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, (E)- (9CI) (CA
INDEX NAME)

Double bond geometry as shown.

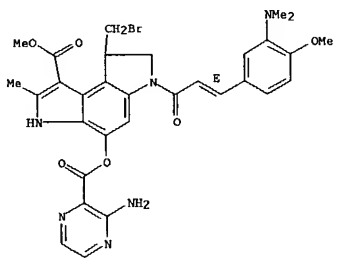
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-39-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[(3-aminopyrazinyl)carbonyl]oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



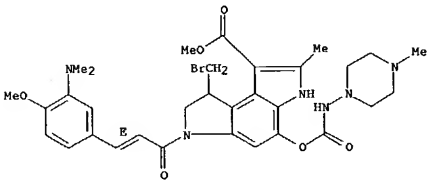
PAGE 2-A

●2 HBr

RN 173088-40-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester,
dihydrobromide, (E)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

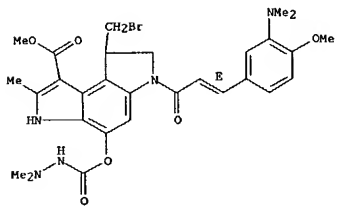
Double bond geometry as shown.



●2 HBr

RN 173088-41-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(2,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

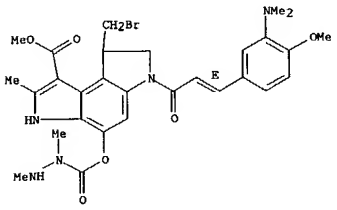


● HBr

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 173088-42-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-4-[[(1,2-dimethylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



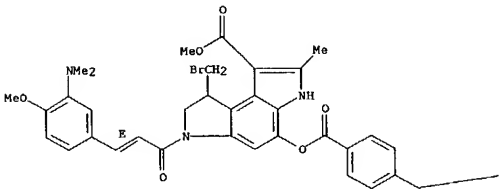
● HBr

RN 173088-43-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[[4-[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester, dihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

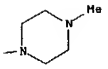
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



● 2 HBr

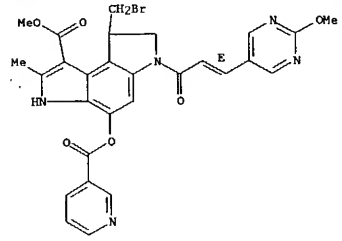
PAGE 1-B



RN 173088-44-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[(3-pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

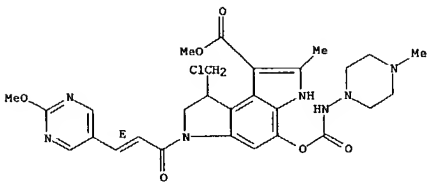
Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 173088-45-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

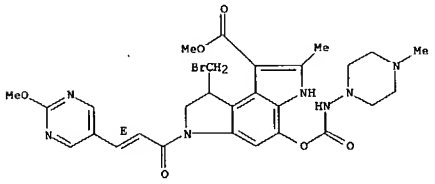


● HCl

RN 173088-46-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrochloride, (E)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

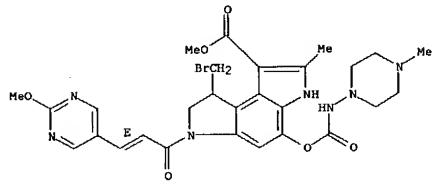
Double bond geometry as shown.



● HCl

RN 173088-47-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[[(4-methyl-1-piperazinyl)amino]carbonyl]oxy]-, methyl ester, monohydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

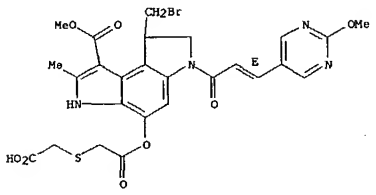


● HBr

RN 173088-48-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[[(carboxymethyl)thio]acetyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, 1-methyl ester, (E)- (9CI) (CA

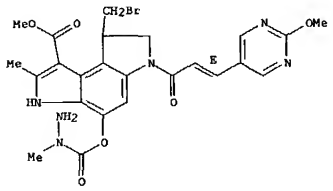
L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Double bond geometry as shown.



RN 173088-49-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-4-[[(1-
methylhydrazino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(2-methoxy-5-
pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-, methyl ester, (E)- (9CI)
(CA
INDEX NAME)

Double bond geometry as shown.

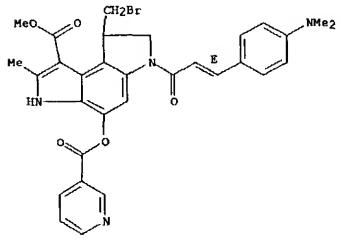


RN 173088-50-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(2-methoxy-5-pyrimidinyl)-1-oxo-2-propenyl]-2-methyl-4-[[4
-

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Double bond geometry as shown.

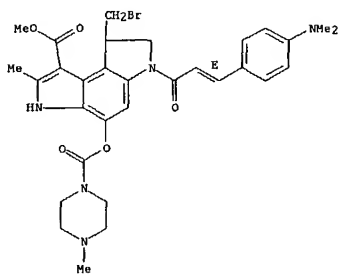


RN 173088-52-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[4-

(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-
[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester,
monohydrobromide,
(E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

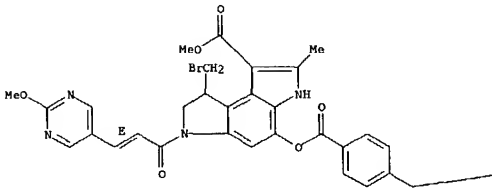
PAGE 1-A



L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(4-methyl-1-piperazinyl)methyl]benzoyl]oxy]-, methyl ester,
monohydrobromide, (E)- (9CI) (CA INDEX NAME)

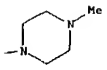
Double bond geometry as shown.

PAGE 1-A



● *HBr*

PAGE 1-B



RN 173088-51-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[4-

(dimethylamino)phenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-methyl-4-[(3-
pyridinylcarbonyl)oxy]-, methyl ester, (E)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

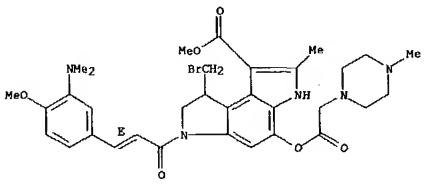
PAGE 2-A

● HBr

RN 173088-55-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-6-[3-[3-

(dimethylamino)-4-methoxyphenyl]-1-oxo-2-propenyl]-3,6,7,8-tetrahydro-2-
methyl-4-[[(4-methyl-1-piperazinyl)acetyl]oxy]-, methyl ester,
trihydrobromide, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



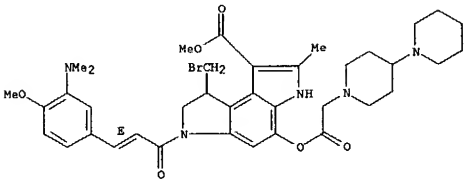
●3 HBr

RN 173088-56-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[[[1,4'-bipiperidin]-1'-

ylacetyl)oxy]-8-(bromomethyl)-6-[3-[3-(dimethylamino)-4-methoxyphenyl]-1-
oxo-2-propenyl]-2-methyl-, methyl ester, trihydrobromide, (E)- (9CI)
(CA
INDEX NAME)

Double bond geometry as shown.

L14 ANSWER 64 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



●3 HBr

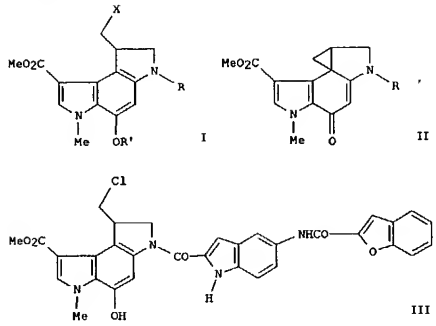
L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:926111 CAPLUS
DN 123:340084
TI Pyrrolo[3,2-e]indole derivatives, process for their preparation, and applications as antitumor agents
IN Delamano Garcia, Jose; Tojo Suarez, Gabriel; Lopez Goti, Carmen; Fernandez Almeida, Jesus; Garcia Gravalos, Dolores; Faircloth, Glynn Thomas
PA Universidad de Santiago de Compostela, Spain
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA Spanish
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9514022	A1	19950526	WO 1994-ES122	19941118
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ES 2074957	A1	19950916	ES 1993-2430	19931119
	ES 2074957	B1	19960616		
	EP 680964	A1	19951108	EP 1995-900773	19941118
	EP 680964	B1	20020116		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08509990	T2	19961022	JP 1994-514236	19941118
	AT 212023	E	20020215	AT 1995-900773	19941118
	PT 680964	T	20020628	PT 1995-900773	19941118
	ES 2171521	T3	20020916	ES 1995-900773	19941118
	US 5786377	A	19980728	US 1997-790904	19970129
PRAI	ES 1993-2430	A	19931119		
	ES 1993-243	A	19930209		
	WO 1994-ES122	W	19941118		
	US 1996-491870	A1	19960515		

OS CASREACT 123:340084; MARPAT 123:340084
GI

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



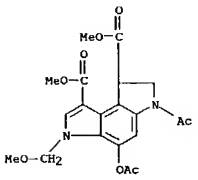
AB New pyrrolo[3,2-e]indole derivs. of formulas I and II are claimed [wherein
R = COR''; R'' = (un)substituted aryl or heteroaryl; R' = H, (un)substituted alkanoyl, alkenoyl, alkynoyl, (hetero)arenocarbonyl; X = Cl, bromo, iodo, alkyl- or arylsulfonyl]. The compds. are prepared by: (a) deacetylating II (R = Ac) to give II (R = H); (b) subjecting the latter to a cyclopropyl ring-opening reaction to give I.HX (R = R' = H); (c) reacting this with an acid R''CO2H to yield I (R = COR'', R' = H); (d) optionally reacting I with a base in the presence of a condensing agent to obtain II; (e) optionally reacting I with a carboxylic acid in the presence of a condensing agent or with an acid chloride in the presence of a base to give I (R' = acyl). I and II are useful as antitumor agents.
For example, deacylation of II (R = Ac) with NaOMe in MeOH gave 99% II (R = H), which was cleaved by anhydrous HCl in EtOAc to give 93% I.HCl (R = R' = H, X = Cl). Coupling of this with 5-[(benzofuran-2-ylcarbonyl)amino]-1H-indole-2-carboxylic acid in DMF in the presence of EtN:C:N(CH2)3NMe2.HCl gave 69% title compound III. In the P388 tumor model in mice, III at 0.5

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

mg/kg/day i.p. for 9 days gave at treated/control survival ratio of > 391%.

IT **170431-06-8P**
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(byproduct; preparation of pyrroloindole derivs. as antitumor agents)

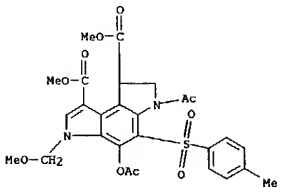
RN 170431-06-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-1,2,3,6-tetrahydro-6-(methoxymethyl)-, dimethyl ester (9CI) (CA INDEX NAME)



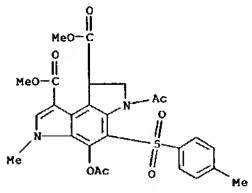
IT **170430-99-6P 170431-00-2P 170431-01-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrroloindole derivs. as antitumor agents)

RN 170430-99-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-1,2,3,6-tetrahydro-6-(methoxymethyl)-4-[(4-methylphenyl)sulfonyl]-, dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

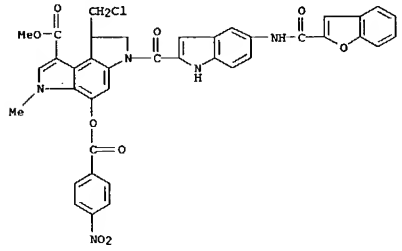


RN 170431-00-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-
1,2,3,6-tetrahydro-6-methyl-4-[(4-methylphenyl)sulfonyl]-, dimethyl ester
(9CI) (CA INDEX NAME)

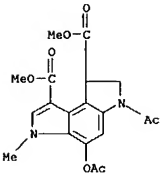


RN 170431-01-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,8-dicarboxylic acid, 3-acetyl-5-(acetyloxy)-
1,2,3,6-tetrahydro-6-methyl-, dimethyl ester (9CI) (CA INDEX NAME)

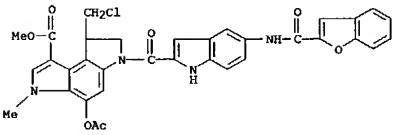
L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 65 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

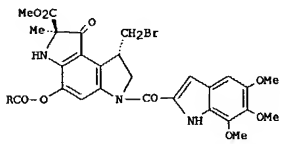


IT 170430-96-3P 170430-97-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrroloindole derivs. as antitumor agents)
RN 170430-96-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-(acetyloxy)-6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 170430-97-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-3-methyl-4-[(4-nitrobenzoyl)oxy]-, methyl ester (9CI)
(CA INDEX NAME)

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:902197 CAPLUS
DN 124:29479
TI Synthesis and antitumor activity of duocarmycin derivatives
AU Nagamura, Satoru; Kanda, Yutaka; Kobayashi, Eiji; Gomi, Katsushige; Saito,
Hiromitsu
CS Kyowa Hakko Kogyo Co., Ltd., Tokyo Res. Lab., Tokyo, 194, Japan
SO Chemical & Pharmaceutical Bulletin (1995), 43(9), 1530-5
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
OS CASREACT 124:29479
GI

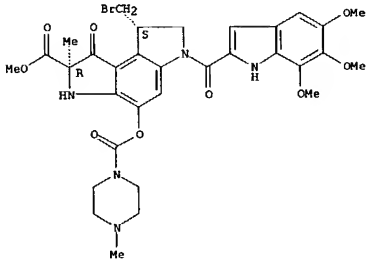


I

AB A series of duocarmycin B2 derivs. I [R = morpholino-, 4-Mepiperazinyl-CO(CH2)n, morpholinyl(CH2)n, PhCH2OCONH(CH2)n, Me2N, 4-Mepiperazinyl, morpholino, piperazinyl, pyrrolidinyl, MeNH, PhNH; n =
1-4], modified at the phenolic hydroxyl group to ester, carbonate and carbamate, was synthesized. Antitumor activity of these analogs was preliminarily evaluated by assays of growth inhibition of HeLa S3 cells
(in vitro) and antitumor activity against murine sarcoma 180 (in vivo).
The stability of the compds. under aqueous conditions was examined, and we found
a correlation between antitumor activity in vivo and stability in aqueous
solution, i.e., the more stable derivs. exhibited higher antitumor activity.
Among these derivs., the N,N-dialkylcarbamoyl analogs exhibited both improved antitumor activity and higher stability compared with duocarmycin
B2. These analogs were subjected to further biol. evaluation and they expressed broad-spectrum activity toward murine solid tumors M5076, Colon
26 and Colon 38, and human xenografted carcinoma MX-1.
IT 154901-65-2P 171524-41-7P 171524-44-0P
171599-18-1P 171599-19-2P 171599-20-5P

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
171599-21-6P 171599-22-7P 171599-23-8P
171599-25-0P 171599-26-1P 171599-27-2P
171599-29-4P 171599-30-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL
(Biological study); PREP (Preparation)
(synthesis, stability and antitumor activity of duocarmycin derivs.)
RN 154901-65-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-
(9CI) (CA INDEX NAME)

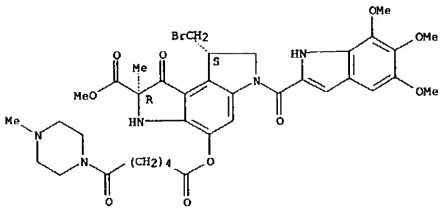
Absolute stereochemistry.



RN 171524-41-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-methyl-1-piperazinyl)-1,6-dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

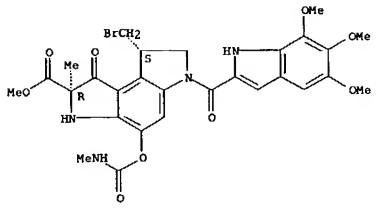
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171524-44-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(methylamino)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
(9CI) (CA INDEX NAME)

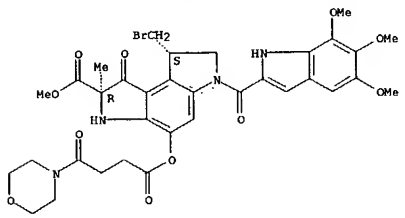
Absolute stereochemistry.



RN 171599-18-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1,4-dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
(9CI) (CA INDEX NAME)

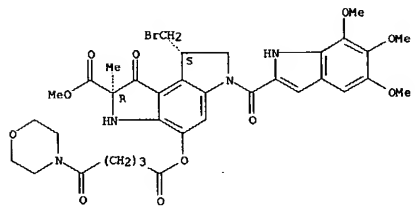
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171599-19-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1,5-dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

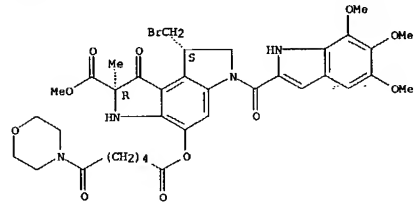
Absolute stereochemistry.



RN 171599-20-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-morpholinyl)-1,6-dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

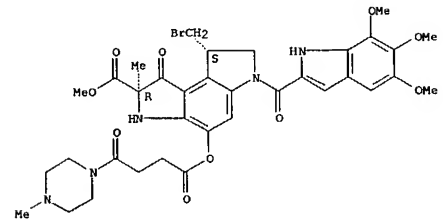
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171599-21-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-methyl-1-piperazinyl)-1,4-dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

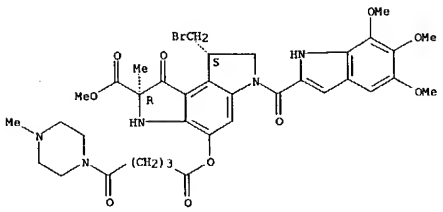
Absolute stereochemistry.



RN 171599-22-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

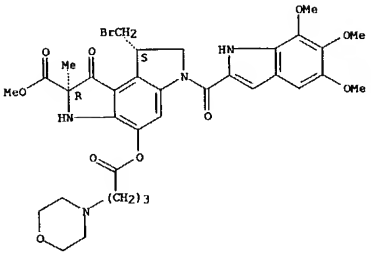
L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



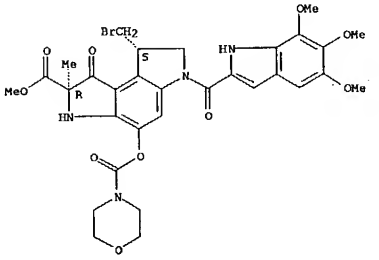
RN 171599-23-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1-oxobutoxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

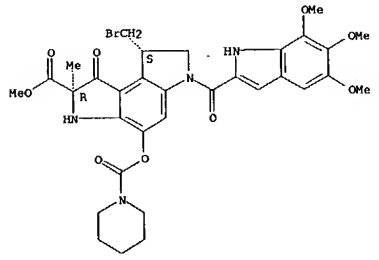


L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 171599-27-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 171599-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-

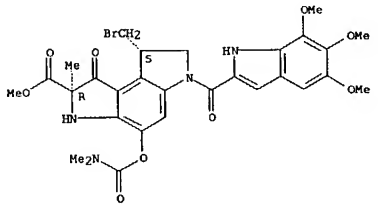
L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HCl

RN 171599-25-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 171599-26-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinylcarbonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

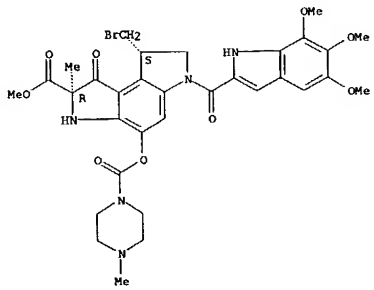
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



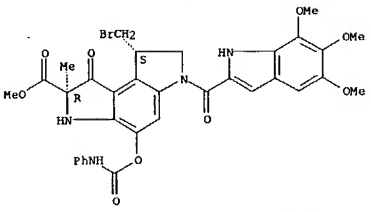
PAGE 2-A

● HCl

RN 171599-30-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[(phenylamino)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

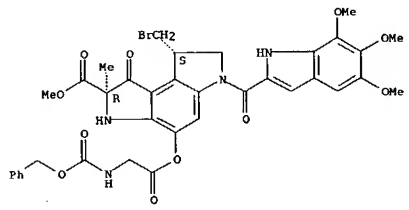
Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **171524-42-8P 171524-43-9P 171599-24-9P**
171599-28-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis, stability and antitumor activity of duocarmycin derivs.)
RN 171524-42-8 CAPLUS
CN Glycine, N-[(phenylmethoxy)carbonyl]-, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl ester, (2R-trans)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

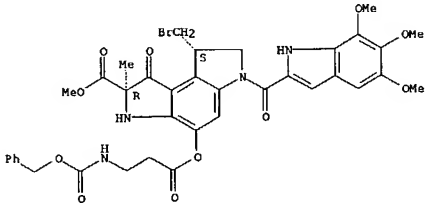


RN 171524-43-9 CAPLUS
CN β-Alanine, N-[(phenylmethoxy)carbonyl]-, 8-(bromomethyl)-1,2,3,6,7,8-

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

hexahydro-2-(methoxycarbonyl)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]benzo[1,2-b:4,3-b']dipyrrol-4-yl ester, (2R-trans)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

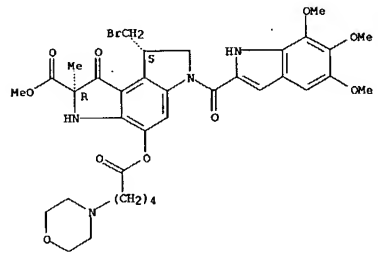


RN 171599-24-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1-oxopentyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 66 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

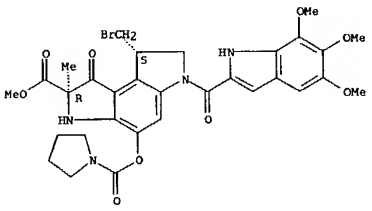


PAGE 2-A

● HCl

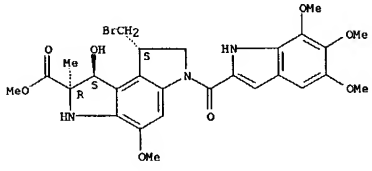
RN 171599-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 67 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:741571 CAPLUS
DN 123:285601
TI Duocarmycins, potent antitumor antibiotics produced by Streptomyces sp.
structures and chemistry
AU Yasuzawa, Tohru; Muroi, Ken'ichi; Ichimura, Michio; Takahashi, Isami; Ogawa, Tatsuhiro; Takahashi, Keiichi; Sano, Hiroshi; Saitoh, Yutaka
CS Tokyo Res. Lab., Tokyo, 194, Japan
SO Chemical & Pharmaceutical Bulletin (1995), 43(3), 378-91
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB Seven novel potent antitumor antibiotics, duocarmycins A, C1, C2, D, B1,
B2 and SA, were isolated from three independently collected Streptomyces
sp. The complete structures, including absolute stereochem., were determined by
spectral and chemical studies of those duocarmycins and several derivs.
Duocarmycins A and SA possess a 1,2,7,7a-tetrahydrocyclopropa[1,2-c]indol-4-one subunit, a common pharmacophore with that of CC-1065 found from Streptomyces zelensis.
IT **169102-68-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(isolation and structures of seven duocarmycins, potent antitumor antibiotics produced by Streptomyces sp.)
RN 169102-68-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [2R-(2α,3α,4β)]-
(9CI) (CA INDEX NAME)

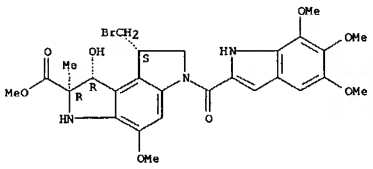
Absolute stereochemistry. Rotation (+).



IT **129953-21-5P 168776-83-8P 168776-86-1P**
168776-88-3P

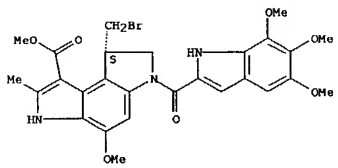
L14 ANSWER 67 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: SPN (Synthetic preparation); PREP (Preparation)
(isolation and structures of seven duocarmycins, potent antitumor antibiotics produced by Streptomyces sp.)
RN 129953-21-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1α,2β,8α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 168776-83-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

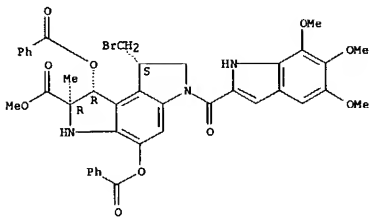
Absolute stereochemistry. Rotation (-).



RN 168776-86-1 CAPLUS

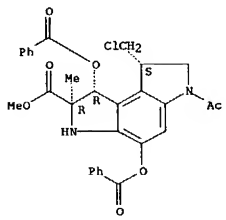
L14 ANSWER 67 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,4-bis(benzoyloxy)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1α,2β,8α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

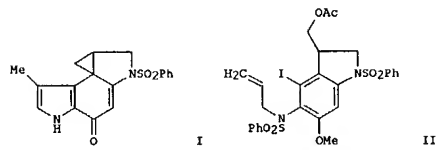


RN 168776-88-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-acetyl-1,4-bis(benzoyloxy)-8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-, methyl ester, [1R-(1α,2β,8α)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



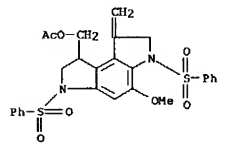
L14 ANSWER 68 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:689509 CAPLUS
DN 123:111712
TI Anticancer agents. 22. Efficient total synthesis of the pharmacophore of the anticancer antibiotic CC-1065 by zirconocene- and palladium-initiated cyclizations
AU Tietze, Lutz F.; Buhr, Wilm
CS Inst. Org. Chem., Univ. Tammannstrasse, Goettingen, D-37077, Germany
SO Angewandte Chemie, International Edition in English (1995), 34(12), 1366-8
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
GI



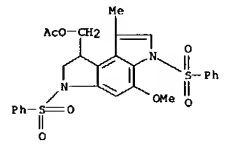
I II

AB The total synthesis of the pharmacophore of CC-1065, I, was achieved via palladium catalyzed cyclization of indole iodide II.
IT **165817-13-0P 165817-15-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of pharmacophore of CC-1065 via zirconocene and palladium-catalyzed cyclizations)
RN 165817-13-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 1,2,3,6,7,8-hexahydro-5-methoxy-8-methylene-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)

L14 ANSWER 68 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



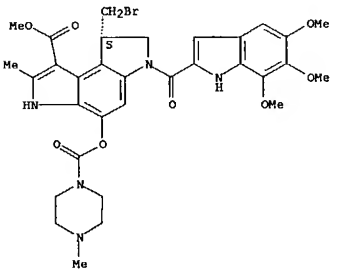
RN 165817-15-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 1,2,3,6-tetrahydro-5-methoxy-8-methyl-3,6-bis(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)



L14 ANSWER 69 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:389254 CAPLUS
DN 122:177804
TI Intracellular carboxyl esterase activity is a determinant of cellular sensitivity to the antineoplastic agent KW-2189 in cell lines resistant to cisplatin and CPT-11
AU Ogasawara, Hayato; Nishio, Kazuto; Kanzawa, Fumihiko; Lee, Yong-Sik; Funayama, Yasunori; Ohira, Tatsuo; Kuraishi, Yasunobu; Isogai, Yukihide; Saijo, Nagahiro
CS Pharmacology Div., National Cancer Center Res. Inst., Tokyo, 104, Japan
SO Japanese Journal of Cancer Research (1995), 86(1), 124-9
CODEN: JJCREP; ISSN: 0910-5050
PB Japanese Cancer Association
DT Journal
LA English
AB KW-2189, a novel antitumor antibiotic belonging to the duocarmycins, possesses marked DNA-binding activity upon activation by carboxyl esterase to its active form, DU-86. Three duocarmycins, KW-2189, DU-86 and duocarmycin SA, were active against the cisplatin (CDDP)-resistant human non-small cell lung cancer cell lines PC-9/CDDP and PC-14/CDDP, and the multidrug-resistant human small cell lung cancer cell line H69/VP. However, HAC2/0.1, a CDDP-resistant human ovarian cancer cell line which is also resistant to CPT-11 because of decreased intracellular activation of CPT-11, was about 12.8-fold more resistant to KW-2189. HAC2/0.1 was not resistant to other duocarmycins as compared to its parental cell line, HAC2. There was no difference between HAC2 and HAC2/0.1 with regard to the intracellular accumulation of KW-2189. Addition of 130 mU/mL of carboxyl esterase to the culture medium did not influence the sensitivity of HAC2 cells to KW-2189. However, the sensitivity of HAC2/0.1 cells to KW-2189 was enhanced to the level of HAC2. These results suggest that HAC2/0.1 is less potent than HAC2 in activating KW-2189. The carboxyl esterase activity of whole-cell and microsomal exts. from HAC2/0.1 was approx. 60% of that from HAC2. The cell-free experiment revealed that KW-2189 bound to DNA more efficiently in the presence of HAC2 than HAC2/0.1 cell extract It was concluded that decreased intracellular carboxyl esterase activity in

L14 ANSWER 69 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
HAC2/0.1 cells caused decreased intracellular conversion of KW-2189 to its active form, thus producing resistance to KW-2189. The decreased conversion of CPT-11 to SN-38 in HAC2/0.1 cells might be explained by decreased carboxyl esterase activity.
IT **154889-68-6**, KW-2189
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(intracellular carboxyl esterase activity as determinant of cellular sensitivity to the antineoplastic agent KW-2189 in cell lines resistant to cisplatin and CPT-11)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

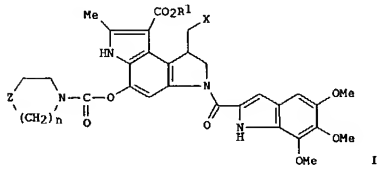
Absolute stereochemistry.



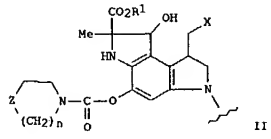
L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:347075 CAPLUS
DN 122:132847
TI Method for preparation of duocarmycin derivatives with antitumor activity
IN Kinugawa, Masahiko; Sakaguchi, Akihiko; Ogasa, Takehiro; Saito, Hiromitsu; Nagamura, Akihito; Tomioka, Shinji
PA Kyowa Hakko Kogyo Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 06298762	A2	19941025	JP 1993-85943	19930413
PRAI JP 1993-85943		19930413		

OS CASREACT 122:132847; MARPAT 122:132847
GI



I

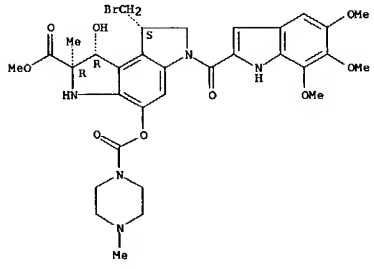


II

AB The title compds. (I; R1 = lower alkyl, allyl, CH2Ph; X = Cl, Br; Z = CH2, O, NR2; wherein R2 = H, lower alkyl; n = 1-4), useful as antitumor agents (no data), are prepared by treating 1,2,3,4-tetrahydro-3H-pyrrolo[3,2-e]indole-7-carboxylic acid derivative (II; R1, X, Z, n = same as above).

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Thus, Me (1S,7R)-1-bromomethyl-7-methyl-5-[(4-methylpiperazinyl)carbonyloxy]-8-oxo-3-[(5,6,7-trimethoxyindol-2-yl)carbonyl]-1,2,7,8-tetrahydro-3H-pyrrolo[3,2-e]indole-7-carboxylate was reduced by NaBH4 in allyl alc. to give, after silica gel chromatog., 63% intermediate II (R1 = Me, X = Br, Z = MeN, n = 2). The latter compd. was stirred with MeSO3H in CH2Cl2 at 47-53° for 5 h to give 86.3% title compd. I (R1 = Me, X = Br, Z = MeN, n = 2).
IT **160819-29-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and dehydration in preparation of duocarmycin derivs. with antitumor activity)
RN 160819-29-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

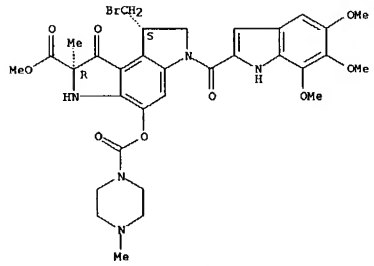


IT **154901-65-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reduction with sodium borohydride in preparation of duocarmycin derivs. with antitumor activity)
RN 154901-65-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-
oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester,
(2R,8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

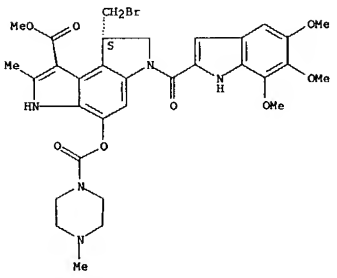


IT **154889-68-6P 160819-28-3P**
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of duocarmycin derivs. with antitumor activity by
acid-catalyzed dehydration of
hydroxytetrahydropyrroloindolecarboxylic
acid derivative)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



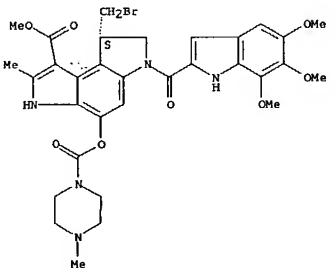
RN 160819-28-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide,
(8S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 70 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



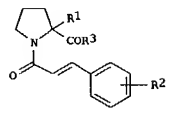
PAGE 2-A

● HBr

L14 ANSWER 71 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:315828 CAPLUS
DN 122:82075
TI N-cinnamoylproline derivatives or alkali metal salts as resolving
agents
for racemate
IN Terajima, Atsuro; Fukuda, Yasumichi
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06293733	A2	19941021	JP 1992-55536	19920313
	JP 3181671	B2	20010703		
PRAI	JP 1992-55536		19920313		

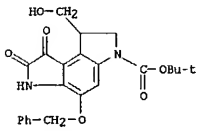
OS MARPAT 122:82075
GI



I

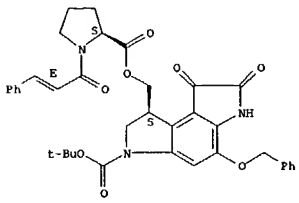
AB N-cinnamoylproline derivs. [I; R1 = H, lower alkyl; R2 = H, halo, OH,
NO2,
lower alkoxy, lower alkyl, (un)substituted Ph; R3 = OH, residue of a
reactive group] or alkali metal salts thereof are used as resolving
agents
of racemates which are difficult to resolve them by conventional
resolving
agents. Thus,
5-benzyloxy-3-(tert-butoxycarbonyl)-1-hydroxymethyl-7,8-
dioxo-1,2,3,6,7,8-hexahydropyrrolo[3,2-e]indole was condensed with
N-cinnamoyl-L-proline in the presence of DCC and
4-dimethylaminopyridine
in CH2Cl2 at room temperature to give a mixture of diastereomer
esters which was
separated by silica gel chromatog. to give 152 mg 5-Benzyloxy-3-(tert-
butoxycarbonyl)-(1S)-(N-cinnamoyl-L-prolyloxymethyl)-7,8-dioxo-1,2,3,6,7,8-
hexahydropyrrolo[3,2-e]indole and 119 mg (1R,S)-diastereomer.
IT **143874-46-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(optical resolution of (hydroxymethyl)hexahydropyrroloindole
derivative by
diastereomer ester formation with N-cinnamoyl-L-proline and silica
gel

L14 ANSWER 71 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
chromatog.)
RN 143874-46-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **149365-69-5P 149365-70-8P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(optical resolution of (hydroxymethyl)hexahydropyrroloindole derivative by
diastereomer ester formation with N-cinnamoyl-L-proline and silica gel
chromatog.)
RN 149365-69-5 CAPLUS
CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)-(9CI)
(CA INDEX NAME)

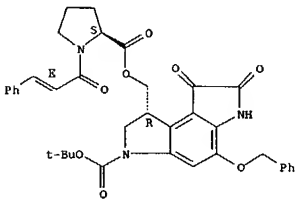
Absolute stereochemistry.
Double bond geometry as shown.



L14 ANSWER 71 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 149365-70-8 CAPLUS
CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

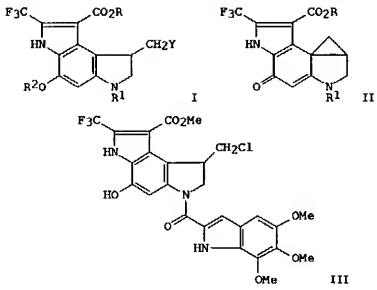


L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:605331 CAPLUS
DN 121:205331
TI preparation of (trifluoromethyl)pyrroloindolecarboxylic esters as antitumor agents
IN Terashima, Shiro; Fukuda, Yasumichi; Oomori, Yasuo
PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9404535	A1	19940303	WO 1993-JP1159	19930819
	W: AU, BB, BG, BR, CA, CZ, FI, HU, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	JP 06116269	A2	19940426	JP 1993-204255	19930818
	JP 3514490	B2	20040331		
	EP 656360	A1	19950607	EP 1994-908108	19930819
	EP 656360	B1	20021120		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	HU 71493	A2	19951128	HU 1995-494	19930819
	AU 689443	B2	19980402	AU 1993-47618	19930819
	AU 9347618	A1	19940315		
	CA 2142869	C	20020101	CA 1993-2142869	19930819
	AT 228132	E	20021215	AT 1994-908108	19930819
	PT 656360	T	20030228	PT 1994-908108	19930819
	ES 2186608	T3	20030701	ES 1994-908108	19930819
	TW 394774	B	20000621	TW 1993-82108171	19931004
	US 5629430	A	19970513	US 1995-381981	19950614
PRAI	JP 1992-222862	A	19920821		
	JP 1993-204255	A	19930818		
	WO 1993-JP1159	W	19930819		

OS MARPAT 121:205331
GI

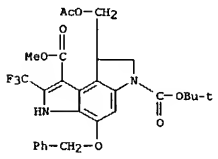
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



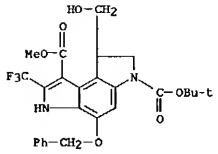
AB The title compds. [I, II; R = alkyl; R1 = α-amino acid residue, etc.; R2 = H, protecting group; Y = halo, arylsulfonyloxy, etc.] are prepared I (R = Me, R1 = Me3CO2C, R2 = H, Y = Cl) was added to 3M HCl-EtOAc
with stirring at room temperature, the residue after distillation was treated with
5,6,7-trimethoxyindole-2-carboxylic acid and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl in DMF with stirring at room temperature under Ar to give
82% III, which showed IC50 of 0.24 ng/mL against P-388 mouse leukemic cells. Also prepared and tested were 103 addnl. I and II.
IT **194093-62-4P 194093-63-5P 194093-64-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, in preparation of antitumor agents)
RN 194093-62-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,

8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

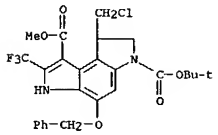
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 194093-63-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 194093-64-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)

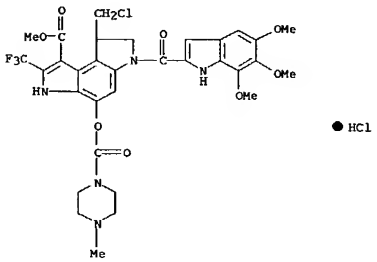


IT **157823-03-5P 157823-04-6P 157823-05-7P**

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

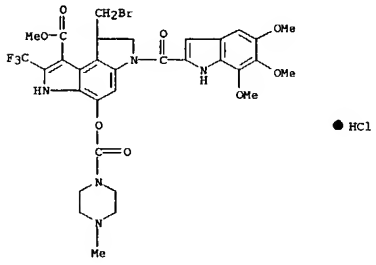
157823-06-8P 157823-08-0P 157823-09-1P
157823-10-4P 157823-11-5P 157823-12-6P
157823-40-0P 157823-41-1P 157823-42-2P
157823-43-3P 157823-44-4P 157823-45-5P
157823-46-6P 157823-47-7P 157823-48-8P
157823-49-9P 157823-50-2P 157823-51-3P
157823-52-4P 157823-53-5P 157823-54-6P
157823-56-8P 157904-26-2P 157904-27-3P
157904-34-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of, as antitumor agent)

RN 157823-03-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-[(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



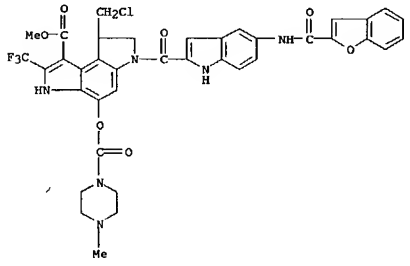
RN 157823-04-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-[(trifluoromethyl)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157823-05-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

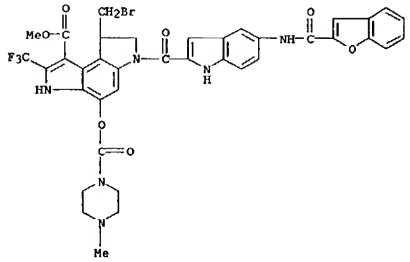


L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

RN 157823-06-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

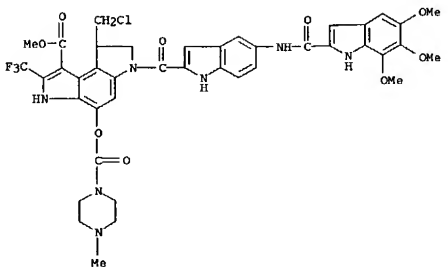
PAGE 1-A



PAGE 2-A

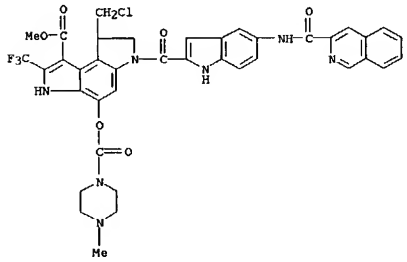
RN 157823-08-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-[[5-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



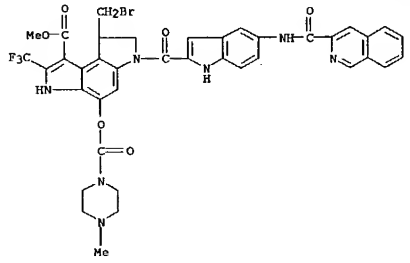
RN 157823-09-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-,
methyl
ester (9CI) (CA INDEX NAME)



L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

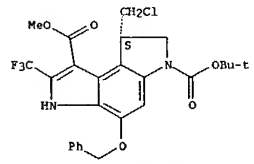


PAGE 2-A

● HCl

RN 157823-12-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,
8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-,
6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



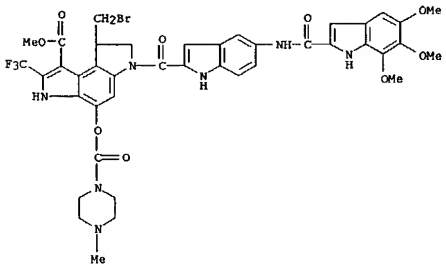
RN 157823-40-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6
-
[(5,6,7-trimethoxy-2-benzofuranyl)carbonyl]-, methyl ester,

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 157823-10-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-
[[5-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1H-indol-2-
yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



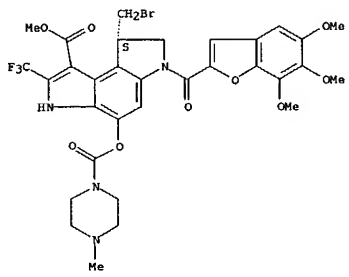
RN 157823-11-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-
4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl
ester, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

● HCl

RN 157823-41-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(chloromethyl)-3,6,7,8-

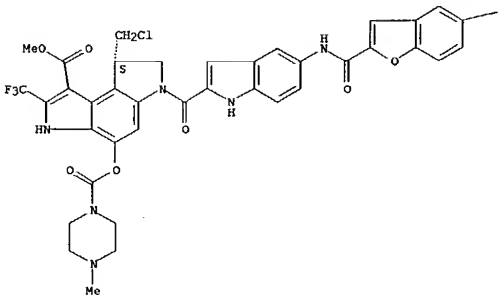
tetrahydro-6-[[5-[[(5-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-

yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-
, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

OMe

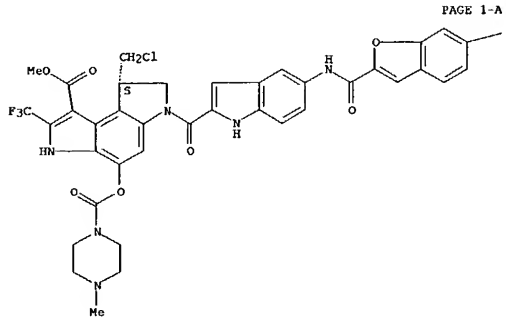
● HCl

RN 157823-42-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(6-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

OMe

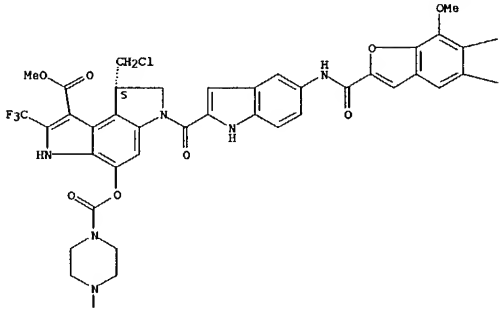
● HCl

RN 157823-43-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
6-[[5-[[(5,6,7-trimethoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

OMe

OMe

PAGE 2-A

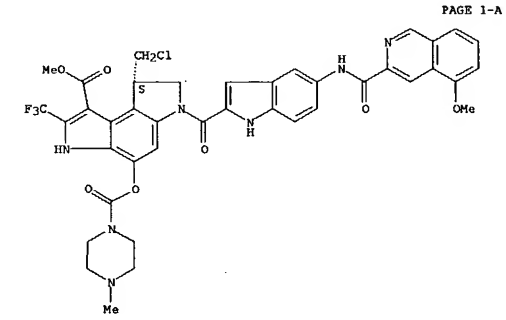
Me

● HCl

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 157823-44-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(5-methoxy-3-isoquinolinyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

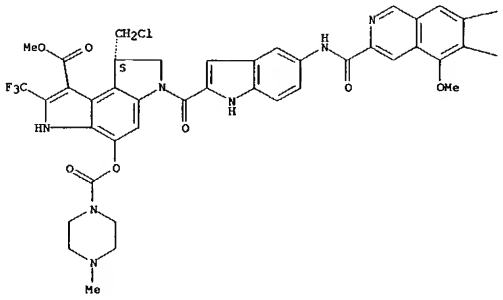
● HCl

RN 157823-45-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-6-[[5-[[(5,6,7-trimethoxy-3-isoquinolinyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

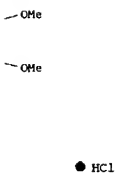
Absolute stereochemistry. Rotation (+).

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



● HCl

RN 157823-46-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[[5-[(9H-pyrido[3,4-

b]indol-3-ylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,

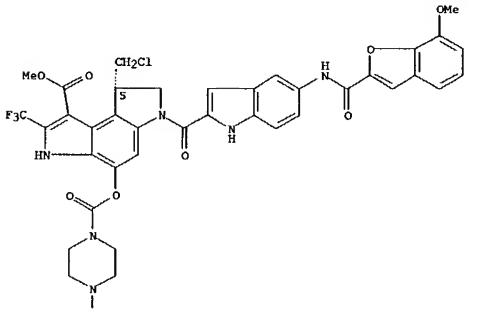
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-

, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 2-A

RN 157823-48-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

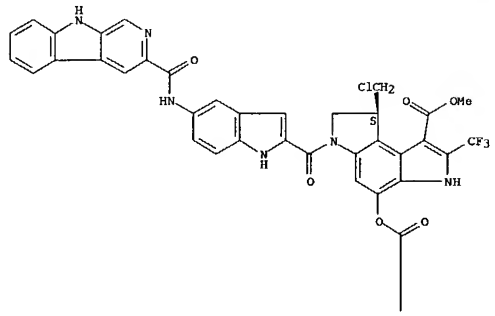
tetrahydro-4-[[[4-(2-hydroxyethyl)-1-piperazinyl]carbonyl]oxy]-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

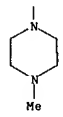
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



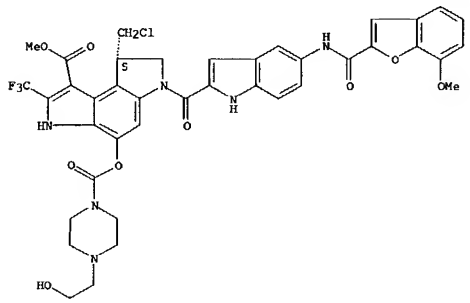
● HCl

RN 157823-47-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

● HCl

RN 157823-49-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

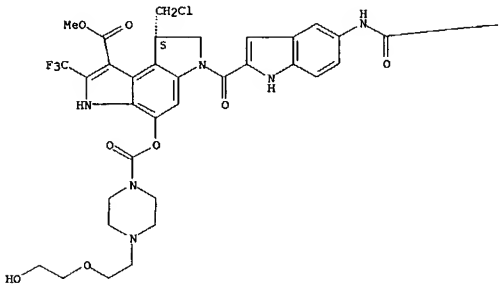
tetrahydro-4-[[[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]carbonyl]oxy]-6-

[[5-[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

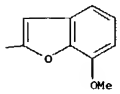
Absolute stereochemistry.

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



● HCl

RN 157823-50-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[1,4'-bipiperidin]-1'-

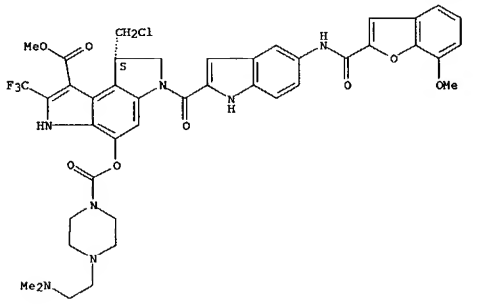
ylcarbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(7-methoxy-2-

benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-(trifluoromethyl)-,

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(trifluoromethyl)-, methyl ester, dihydrochloride, (S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

●2 HCl

RN 157823-52-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 4-[[[4-(2-aminoethyl)-1-

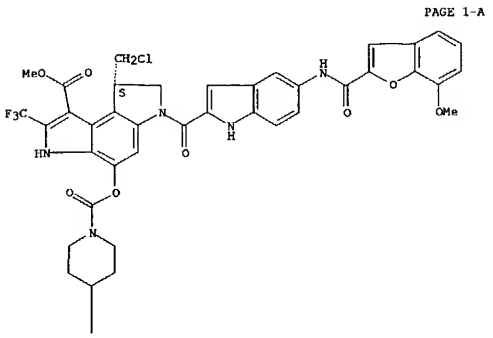
piperazinyl]carbonyl]oxy]-8-(chloromethyl)-3,6,7,8-tetrahydro-6-[[5-[[(7-
methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
(trifluoromethyl)-, methyl ester, dihydrochloride, (S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl ester, monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

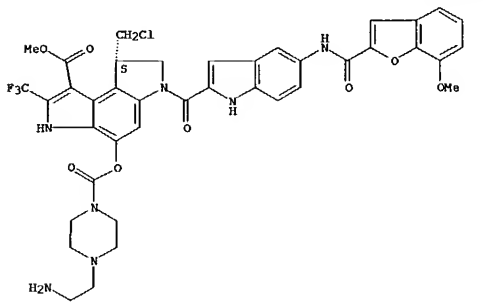
● HCl

RN 157823-51-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[4-[2-

(dimethylamino)ethyl]-1-piperazinyl]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-
[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

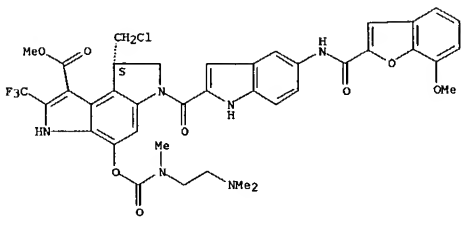
●2 HCl

RN 157823-53-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[[[2-

(dimethylamino)ethyl]methylamino]carbonyl]oxy]-3,6,7,8-tetrahydro-6-[[5-
[[(7-methoxy-2-benzofuranyl)carbonyl]amino]-1H-indol-2-yl]carbonyl]-2-
(trifluoromethyl)-, methyl ester, monohydrochloride, (S)- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

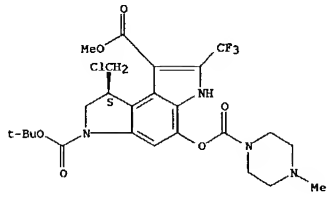


● HCl

RN 157823-54-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,

8-(chloromethyl)-7,8-dihydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

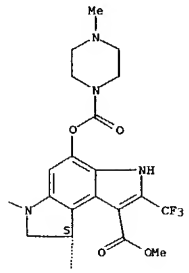


RN 157823-56-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 6,6'-[carbonylbis(imino-1H-

indole-5,2-diylcarbonyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[(4-

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



PAGE 2-A

PAGE 2-B

RN 157904-26-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,

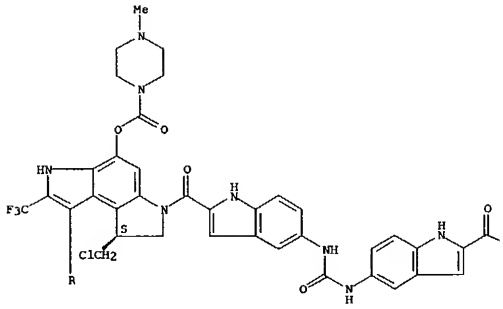
8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

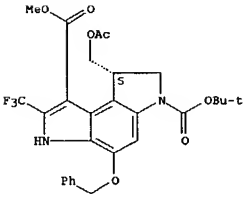
L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, dimethyl ester,
[S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

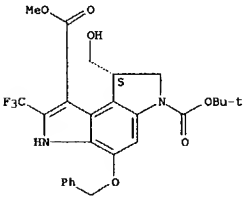


L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157904-27-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-2-(trifluoromethyl)-, 6-(1,1-dimethylethyl) 1-methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



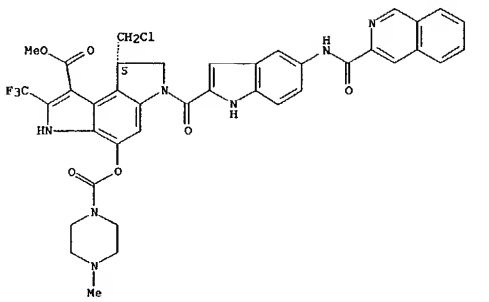
RN 157904-34-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

tetrahydro-6-[[5-[(3-isoquinolinylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-2-(trifluoromethyl)-, methyl ester, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L14 ANSWER 72 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

● HCl

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1994:557348 CAPLUS

DN 121:157348

TI Synthetic studies on duocarmycin. 2. Synthesis and cytotoxicity of natural
(+)-duocarmycin A and its three possible stereoisomers

AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Terashima, Shiro

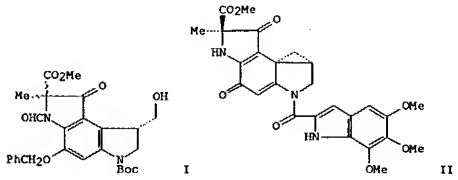
CS Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi, 329-01, Japan

SO Tetrahedron (1994), 50(9), 2809-20
CODEN: TETRAB; ISSN: 0040-4020

DT Journal

LA English

GI



I II

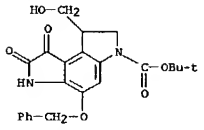
AB The title synthesis was achieved by featuring the optical resolution of two
types of the tricyclic intermediates, e.g., I, and the synthetic scheme
established in the synthesis of racemic compds. In vitro cytotoxicity assay against P388 murine leukemia obviously showed that the absolute configuration of cyclopropane moiety in (+)-duocarmycin A (II) is closely
related to its cytotoxicity.

IT **143874-46-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with cinnamoylproline)

RN 143874-46-8 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-
(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

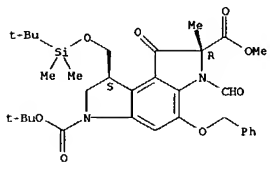


IT **132628-67-2 132628-68-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(desilylation of)

RN 132628-67-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

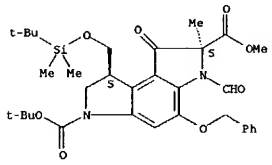


RN 132628-68-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

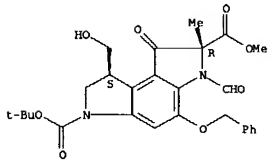


IT **149365-66-2P 149365-67-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and condensation of, with acetylmandelic acid)

RN 149365-66-2 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA
INDEX NAME)

Relative stereochemistry.

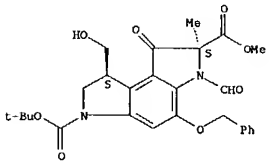


RN 149365-67-3 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid, 6-formyl-1,6,7,8-tetrahydro-1-(hydroxymethyl)-7-methyl-8-oxo-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) 7-methyl ester, cis- (9CI) (CA
INDEX NAME)

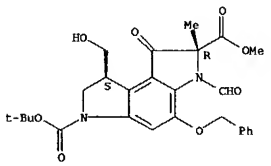
Relative stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **157478-14-3P 157478-15-4P 157478-16-5P**
157478-17-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to
(indolylcarbonyl)benzodipyrrolecarboxylat
e)
RN 157478-14-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)-
(9CI)
(CA INDEX NAME)

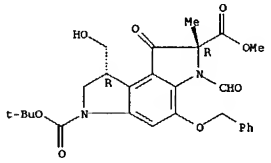
Absolute stereochemistry.



RN 157478-15-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-trans)-
(9CI)
(CA INDEX NAME)

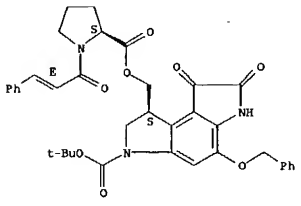
Absolute stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **149365-69-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to ester)
RN 149365-69-5 CAPLUS
CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-
dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-
(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)-
(9CI)
(CA INDEX NAME)

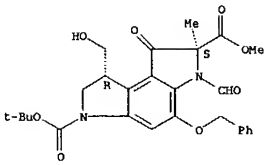
Absolute stereochemistry.
Double bond geometry as shown.



IT **157478-20-1P 157478-21-2P 157478-22-3P**
157478-23-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(preparation and debenzylation of)
RN 157478-20-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
1,2,3,6,7,8-hexahydro-2-

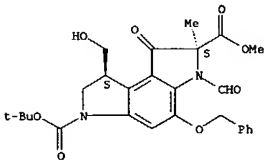
methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI)
(CA

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157478-16-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-cis)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

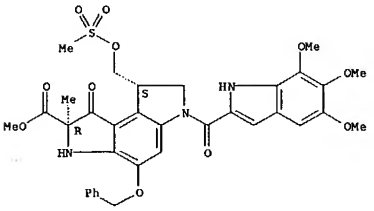


RN 157478-17-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-
(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-cis)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

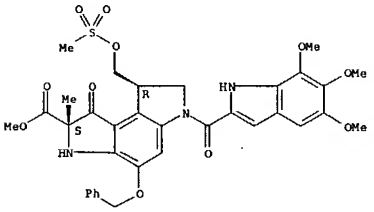
Absolute stereochemistry. Rotation (+).



RN 157478-21-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
1,2,3,6,7,8-hexahydro-2-

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry. Rotation (-).

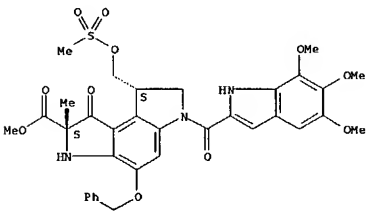


RN 157478-22-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
1,2,3,6,7,8-hexahydro-2-

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI)
(CA

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

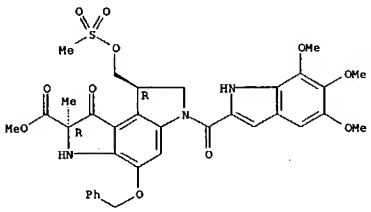
Absolute stereochemistry. Rotation (-).



RN 157478-23-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-cis)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry. Rotation (+).

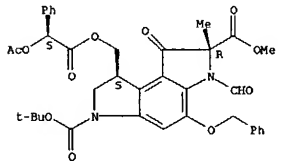


IT **157478-33-6P 157478-34-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 149365-68-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester,
[2R-[2α,8β(S*)]]- (9CI) (CA INDEX NAME)

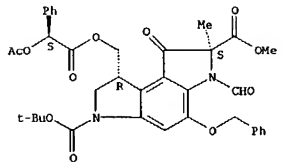
Absolute stereochemistry. Rotation (+).



RN 149405-52-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2S-[2α,8β(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

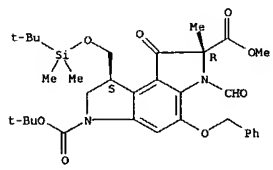


RN 149405-56-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2S-[2α,8α(R*)]]- (9CI) (CA INDEX NAME)

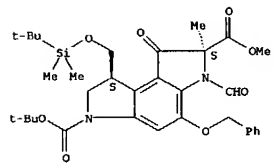
L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Reactant or reagent)
(prepn. and desilylation of)
RN 157478-33-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



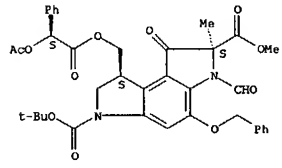
RN 157478-34-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **149365-68-4P 149405-52-7P 149405-56-1P 149405-57-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrolysis of)

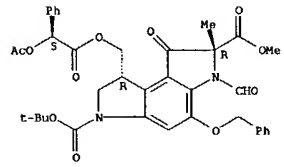
L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).



RN 149405-57-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2R-[2α,8α(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

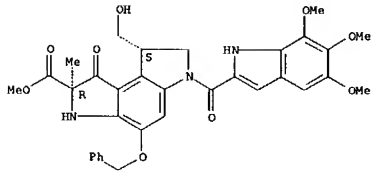


IT **149405-53-8P 149405-54-9P 157478-18-7P 157478-19-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and mesylation of)
RN 149405-53-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

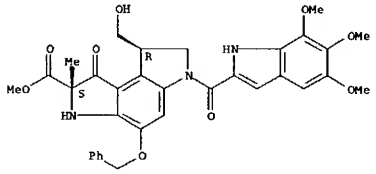
L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149405-54-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

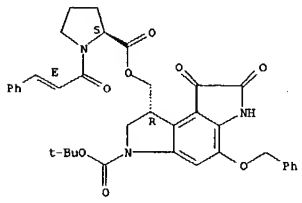


RN 157478-18-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

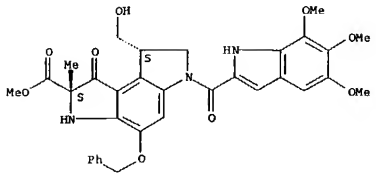
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



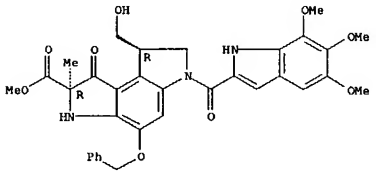
L14 ANSWER 73 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 157478-19-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-cis)- (9CI) (CA INDEX NAME)

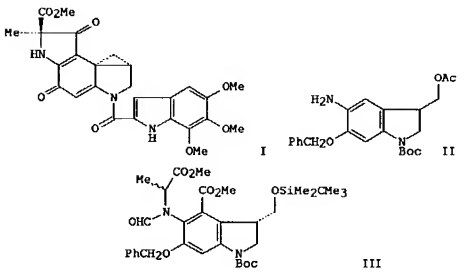
Absolute stereochemistry. Rotation (+).



IT **149365-70-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 149365-70-8 CAPLUS
CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:557347 CAPLUS
DN 121:157347
TI Synthetic studies on duocarmycin. 1. Total synthesis of dL-duocarmycin A
and its 2-epimer
AU Fukuda, Yasumichi; Itoh, Yoshio; Nakatani, Kazuhiko; Terashima, Shiro
CS Sagami Chem. Res. Cent., Kanagawa, 229, Japan
SO Tetrahedron (1994), 50(9), 2793-808
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 121:157347
GI

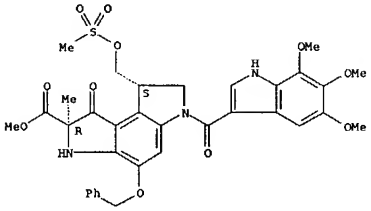


AB The title synthesis of dL-duocarmycin A (I) and its 2-epimer was first achieved by employing novel methoxycarbonylation of the C4-position of the
5-aminoindoline II by way of the isatin and subsequent Dieckmann cyclization of indolecarboxylate III to the Me 2-methylindoxyl-2-carboxylate as key steps. In vitro cytotoxicity assay against P388 murine
leukemia obviously disclosed that cytotoxicities of the synthesized compds. are comparable and almost half of that of natural (+)-duocarmycin
A.
IT **157485-12-6P 157485-13-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenation of)
RN 157485-12-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

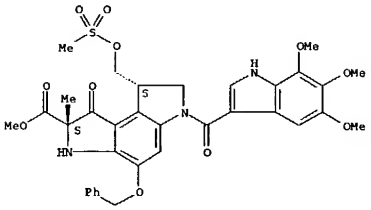
Relative stereochemistry.



RN 157485-13-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

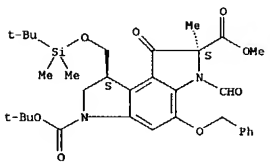
Relative stereochemistry.



L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

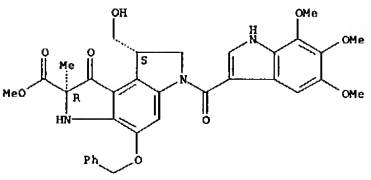
Relative stereochemistry.



IT **157485-10-4P 157485-11-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mesylation of)
RN 157485-10-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



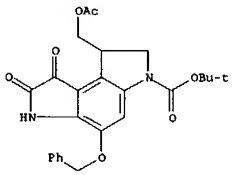
RN 157485-11-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-3-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

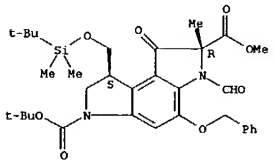
L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **132628-62-7P 132628-67-2P 132628-68-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
RN 132628-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-
1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



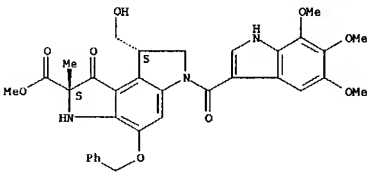
RN 132628-67-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

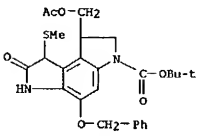


RN 132628-68-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

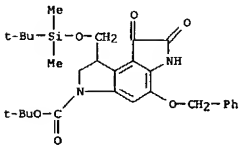
L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **132628-61-6P 132628-63-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)
RN 132628-61-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-
1,6,7,8-tetrahydro-8-(methylthio)-7-oxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

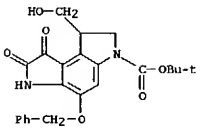


RN 132628-63-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 74 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

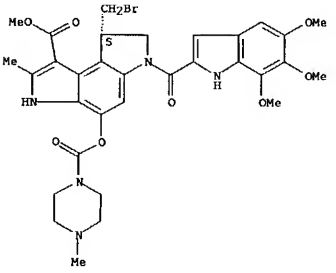
IT **143874-46-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and silylation of)
RN 143874-46-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 75 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:548428 CAPLUS
DN 121:148428
TI A novel antitumor antibiotic, KW-2189, is activated by carboxyl esterase and induces DNA strand breaks in human small cell lung cancer cells
AU Ogasawara, Hayato; Nishio, Kazuto; Takeda, Yuichiro; Ohmori, Tohru; Kubota, Naohiro; Funayama, Yasunori; Ohira, Tatsuo; Kuraishi, Yasunobu; Isogai, Yukihide; Saijo, Nagahiro
CS Pharmacol. Div., Natl. Cancer Center Res. Inst., Tokyo, 104, Japan
SO Japanese Journal of Cancer Research (1994), 85(4), 418-25
CODEN: JJCREP; ISSN: 0910-5050
DT Journal
LA English
AB The purpose of this study was to examine the DNA-binding potency and the mechanisms of cytotoxicity of KW-2189. In order to analyze the DNA-binding activity of KW-2189, plasmid pBR322 was treated with KW-2189 with or without pretreatment with carboxyl esterase, and the products were examined by agarose gel electrophoresis and restriction enzyme anal. Cytotoxic activity was examined by exposing a human small-cell lung cancer cell line, NCI-H69, to KW-2189 with or without carboxyl esterase. Alkaline elution was performed to examine whether KW-2189 induces DNA strand breaks. DNA treated with KW-2189 and carboxyl esterase migrated faster than DNA treated with KW-2189 alone, which migrated at the same rate as untreated DNA. In addition DNA treated with esterase-activated KW-2189 was protected from digestion by some restriction enzymes. KW-2189 had concentration- and time-dependent growth inhibitory effects, with IC50 values from 58 nM (96 h) to 1900 nM (1 h) in H69 cells. The IC50 values for 4-h exposure of H69 to KW-2189 plus 0, 26, 130, and 650 mU carboxyl esterase/mL were 460, 120, 30, and 7 nM, resp. Time-dependent enhancement of cytotoxicity by carboxyl esterase was also observed KW-2189 induced DNA strand breaks in H69 cells in a concentration-dependent manner around the IC50 value. Apparently: (1) KW-2189 is activated by carboxyl esterase to its active form(s); (2) activated KW-2189 has a stronger DNA-binding activity and cytotoxicity than KW-2189 alone; (3) DNA cleavage is one of the major mechanisms of KW-2189-mediated cytotoxicity.
IT **154889-68-6**, KW 2189

L14 ANSWER 75 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neoplasm inhibition by, DNA damage as mechanism of, activation in relation to)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

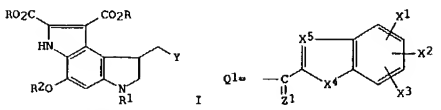
Absolute stereochemistry.



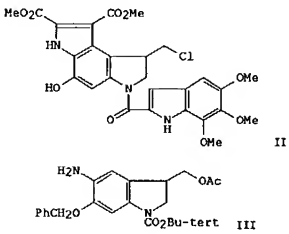
L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:508766 CAPLUS
DN 121:108766
TI Preparation of tetrahydropyrroloindoles as antitumor agents
IN Terajima, Atsuro; Fukuda, Yasumichi; Oomori, Yasuo
PA Kyorin Seiyaku Kk, Japan; Sagami Chem Res
SO Jpn. Kokai Tokkyo Koho, 21 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06122684	A2	19940506	JP 1992-274282	19921013
PRAI	JP 1992-274282		19921013		

OS MARPAT 121:108766
GI



I

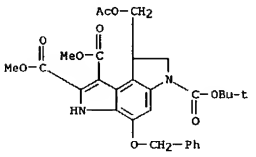


II

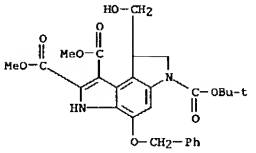
III

AB The title compds., e. g., I [R = alkyl; R1 = Q1, etc.; X4 = O, S, NH; X5 = CH, N; X1 - X3 = H, OH, etc.; Z1 = O, S, etc.; R2 = H, OH-protecting group, etc.; Y = halo, etc.] are prepared The title compound II was prepared in multiple steps from indoline derivative III. II in vitro showed IC50 of 0.31 ng/mL against P388 mouse leukemic cells.
IT **156905-81-6P 156905-82-7P 156905-83-8P**

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and reaction of, in prepn. of antitumor agent)
RN 156905-81-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1,2-dimethyl ester (9CI) (CA INDEX NAME)



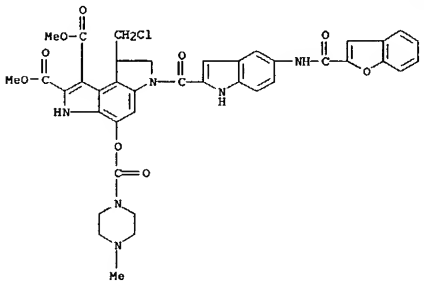
RN 156905-82-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
1,2-dimethyl ester (9CI) (CA INDEX NAME)



RN 156905-83-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2,6(3H)-tricarboxylic acid, 8-(chloromethyl)-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
1,2-dimethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 156905-77-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl
ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A

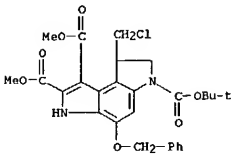


PAGE 2-A

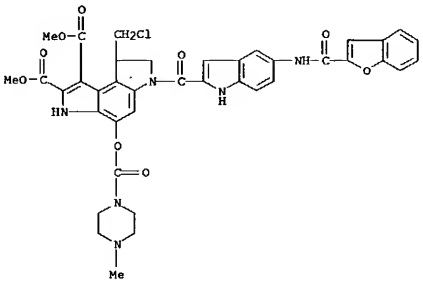
● HCl

RN 156905-78-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl
ester (9CI) (CA INDEX NAME)

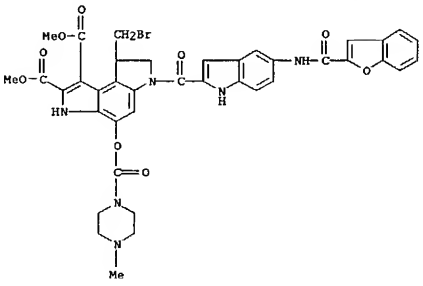
L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 156905-76-9P 156905-77-0P 156905-78-1P
156905-79-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antitumor agent)
RN 156905-76-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(chloromethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl
ester (9CI) (CA INDEX NAME)

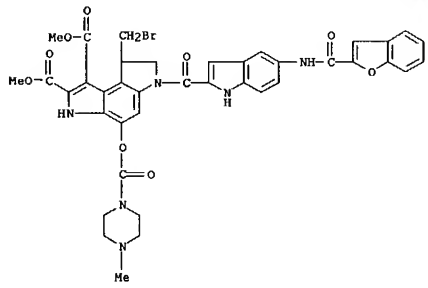


L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 156905-79-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,2-dicarboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-3,6,7,8-tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, dimethyl
ester, monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



L14 ANSWER 76 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

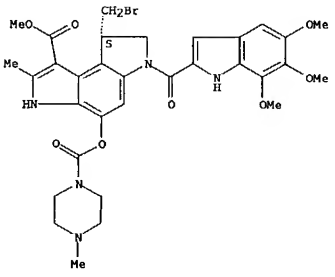
PAGE 2-A

● HCl

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
compd. was deacetylated with K2CO3 in MeOH and chlorinated by CCl4 and
PPh3 in CH2Cl2 at room temp. to give (3S)-I (R3 = PhCH2, R4 = Me3CO2C, X1
= Cl) which was converted into (S)-KW-2189 II in 5 steps.
IT **156395-56-1**, KW 2189
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediates for, tetrahydropyrroloindole derivs. as)
RN 156395-56-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

● HCl

IT **156295-27-1P 156295-32-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and chlorination of, by carbon tetrachloride and triphenylphosphine)
RN 156295-27-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid,

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:483318 CAPLUS
ON 121:83318
TI Preparation of tetrahydropyrroloindole derivative and intermediates therefor
IN Terashima, Shiro; Fukuda, Yasumichi
PA Kyorin Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

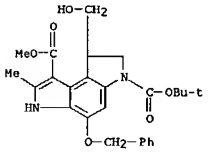
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9404534	A1	19940303	WO 1993-JP1158	19930819
W: AU, BB, BG, BR, CA, CZ, FI, HU, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 06116270	A2	19940426	JP 1993-204254	19930818
AU 9349811	A1	19940315	AU 1993-49811	19930819
PRAI JP 1992-222861	A	19920821		
JP 1993-204254	A	19930818		
WO 1993-JP1158	W	19930819		

OS CASREACT 121:83318; MARPAT 121:83318
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

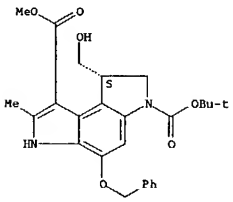
AB Tetrahydropyrroloindole derivs. (I; R1 = H or a hydroxyl-protecting group; R2 = H or an amino-protecting group; X = halo, OH, alkylcarbonyloxy, arylcarbonyloxy, alkylsulfonyloxy, arylsulfonyloxy) and optically active isomers thereof, useful as intermediates for a prospective anticancer agent KW-2189 (II.HCl), are prepared by reaction of aminoindoline derivs. (III; R = H; R3 = HO-protective group; R4 = H2N-protective group; X1 = protected HO) with MeC.tplbond.CCO2Me, MeCOCH2CO2Me, or substituted Me crotonate and cyclization of the resulting Me (indolinylamino)crotonate
III (R = CMe:CHCO2Me; R3, R4, X1 = same as above) in the presence of a metal catalyst. Thus, (3S)-III (R = H, R3 = PhCH2, R4 = Me3CO2C, X1 = OAc), MeCOCH2CO2Me, and p-MeC6H4SO3H.H2O were refluxed in benzene at 80° for 4 h to give (3S)-III (R = CMe:CHCO2Me; R3, R4, X1 = same as above) which was heated in the presence of Pd(OAc)2 in DMF at 70° for 4 h to give (3S)-I (R3 = PhCH2, R4 = Me3CO2C, X1 = OAc). The latter

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



RN 156295-32-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

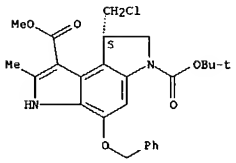
Absolute stereochemistry.



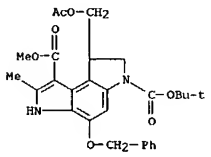
IT **156295-33-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
USES (Uses)
(preparation and conversion of, into anticancer KW-2189)
RN 156295-33-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



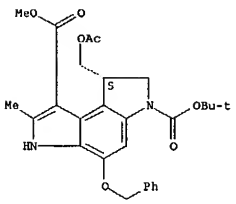
IT **156295-26-0P 156295-31-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and deacetylation of)
RN 156295-26-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



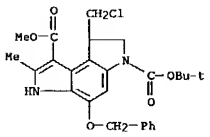
RN 156295-31-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-[(acetyloxy)methyl]-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



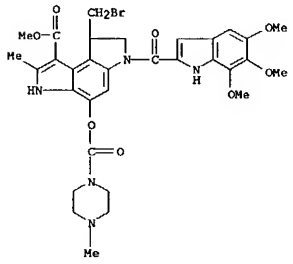
IT **156295-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenolysis of)
RN 156295-29-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1,6(3H)-dicarboxylic acid, 8-(chloromethyl)-7,8-dihydro-2-methyl-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 1-methyl ester (9CI) (CA INDEX NAME)



IT **134106-78-8P 134106-80-2P 154889-68-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as anticancer agent)
RN 134106-78-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

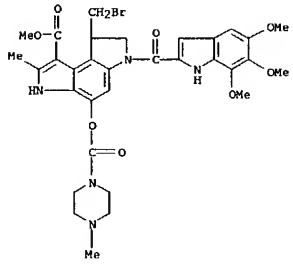
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-

L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134106-80-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI)
(CA INDEX NAME)

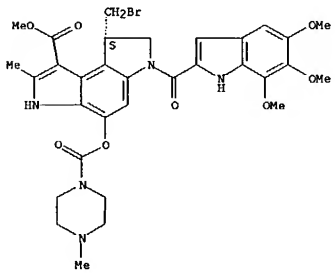


● HCl

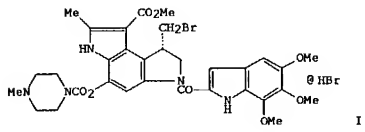
L14 ANSWER 77 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 78 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:315371 CAPLUS
DN 120:315371
TI Characteristics of antitumor activity of KW-2189, a novel water-soluble
derivative of duocarmycin, against murine and human tumors
AU Kobayashi, Eiji; Okamoto, Akihiko; Asada, Masao; Okabe, Masami; Nagamura,
Satoru; Asai, Akira; Saito, Hiromitsu; Gomi, Katsushige; Hirata, Tadashi
CS Pharm. Res. Lab., Kyowa Hokko Kogyo Co., Ltd., Nagaizumi, 411, Japan
SO Cancer Research (1994), 54(9), 2404-10
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
GI



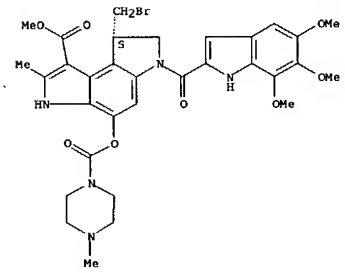
I

AB KW-2189 (I), a novel derivative of duocarmycin B2, was selected for extensive
evaluation based on its improved antitumor activity, water solubility, and
stability in the culture medium, as compared with duocarmycin B2. Although the in vitro cell growth-inhibitory activity of KW-2189 was less
potent than that of duocarmycin B2, it significantly inhibited the growth
of five murine solid tumors including Colon 26 adenocarcinoma, Colon 38
adenocarcinoma, and B16 melanoma in vivo. KW-2189 was also effective
against murine P388 leukemia and L1210 leukemia not only by local
administration (i.p.-i.p. system), but also by systemic administration
(i.p.-i.v. or i.v.-i.v. system). The most remarkable feature of KW-2189
was its efficacy against various human xenografts, which was observed in 14
tumors among 16 tested tumors including drug-insensitive tumors by single
i.v. administration. Tumor regression was observed in mice bearing LC-6

L14 ANSWER 78 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
lung, St-4 and St-40 stomach, Li-7 liver, PAN-2 pancreas, and MX-1 breast
carcinomas. In many cases, the activities of KW-2189 were more than those
of clin. active agents, mitomycin C, Adriamycin, cisplatin, and
cyclophosphamide. Delayed lethal toxicity, which was reported in mice
treated with CC-1065 whose structure was similar to KW-2189, was not obsd.
in mice treated with KW-2189. KW-2189 inhibited DNA synthesis more
significantly than RNA or protein synthesis, although DNA strand breaks
were not obsd. KW-2189 was activated by porcine liver esterase, mouse
liver homogenate or Hep G2 homogenate, and DU-86-DNA adducts were detected
in KW-2189-treated HeLa S3 cells, suggesting that KW-2189 was converted to
DU-86 in the cells. These results indicate that KW-2189 is an interesting
candidate for further development as a novel antitumor agent.
IT **154889-68-6**, KW 2189
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(antitumor activity of, in human and laboratory animal)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

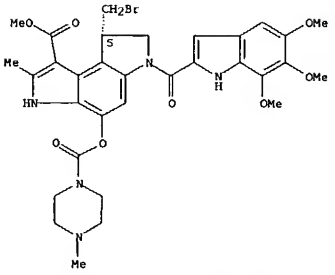
L14 ANSWER 78 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:315183 CAPLUS
DN 120:315183
TI A Novel Property of Duocarmycin and Its Analogs for Covalent Reaction with
DNA
AU Asai, Akira; Nagamura, Satoru; Saito, HIromitsu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., Machida, 194,
Japan
SO Journal of the American Chemical Society (1994), 116(10), 4171-7
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB For understanding the mechanism of action of antitumor agents and
designing new drugs, the DNA alkylating property of duocarmycin (DUM) and
its analogs was examined The thermal depurination products of calf thymus
DNA covalently bonded to DUMA were revealed to be not only the DUMA-N3
adenine adduct but also unexpectedly the DUMA-N3 guanine adduct. In addition
DUMSA and 2 synthetic analogs with higher solvolytic stability, reacted
more selectively with N3 adenine than DUMA did. The correlation between
electrophilicity of the cyclopropanesubunit in the mol. and selectivity to
adenine was observed KW-2189, a synthetic derivative which has improved in vivo
antitumor activity, was designed as a prodrug requiring enzymic hydrolysis
of the carbamoyl moiety, followed by the drug regeneration. Surprisingly
the authors discovered that KW-2189 itself alkylated DNA covalently
without release of the carbamoyl moiety. For the mechanism of DNA
alkylation by KW-2189, a novel alkylating reaction via the formation of an
iminium intermediate without loss of the carbamoyl moiety was proposed.
IT **154889-68-6**, KW 2189
RL: PRP (Properties)
(DNA alkylating property of, structure effect on)
RN 154889-68-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (8S)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

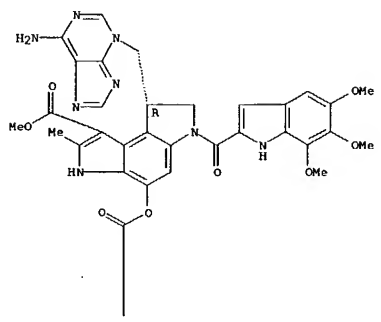


IT **154715-67-0 154715-68-1 154901-65-2**
RL: FORM (Formation, nonpreparative)
(formation of, antitumor activity in relation to)
RN 154715-67-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-[(6-amino-3H-purin-3-yl)methyl]-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (R)- (9CI) (CA INDEX NAME)

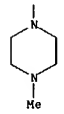
Absolute stereochemistry.

L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



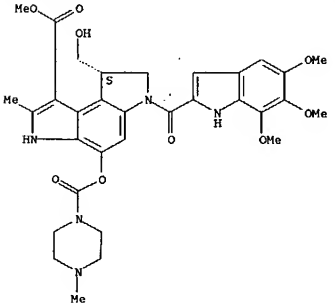
PAGE 2-A



RN 154715-68-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 3,6,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

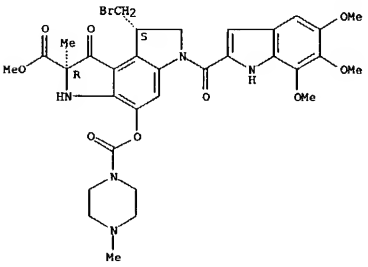
Absolute stereochemistry.

L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 154901-65-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



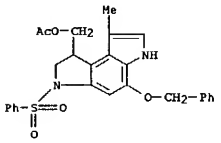
L14 ANSWER 79 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L14 ANSWER 80 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:217053 CAPLUS
DN 120:217053
TI Synthesis of (±)-N2-(benzenesulfonyl)-CPI, the protected A-unit of the
antitumor antibiotic CC-1065, by two metal-initiated cyclizations
AU Tietze, Lutz F.; Grote, Thomas
CS Inst. Org. Chem., Georg-August-Univ., Goettingen, D-37077, Germany
SO Journal of Organic Chemistry (1994), 59(1), 192-6
CODEN: JOCRAH; ISSN: 0022-3263
DT Journal
LA English
OS CASREACT 120:217053
GI

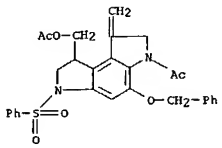
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A new synthetic route to (±)-N2-(Benzenesulfonyl)-CPI (I), the protected A-unit containing a cyclopropylhexadienone moiety of the highly potent antitumor antibiotic CC-1065, from 5-(benzyloxy)-2-bromophenylamine is described. The key steps are a zirconium- and a palladium-initiated cyclization to give the two pyrrole moieties. Reaction of N-allyl-N-(benzenesulfonyl)bromophenylamine II with zirconocene(methyl) chloride leads after workup with I2 to the 4-iodoindoline III, which was transformed into (allylamino)iodoindole IV and subsequently via Heck reaction into the pyrroloindoline V.
IT **153914-88-6 153914-89-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as intermediate, synthesis of (benzenesulfonyl)-CPI)
RN 153914-88-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 6-acetyl-1,2,3,6,7,8-hexahydro-8-methylene-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester) (9CI)
(CA INDEX NAME)

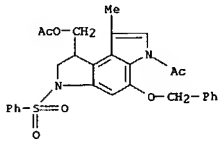
L14 ANSWER 80 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 80 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 153914-89-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 6-acetyl-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester) (9CI) (CA
INDEX NAME)

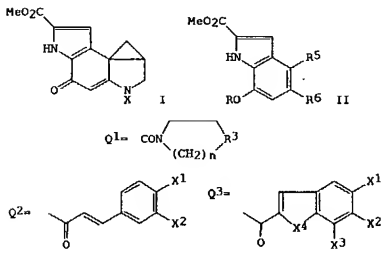


IT **153914-90-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate, synthesis of (benzenesulfonyl)-CPI)
RN 153914-90-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:163825 CAPLUS
DN 120:163825
TI Preparation of DC 113 derivatives as antitumor or antimicrobial agents
IN Nagamura, Akihito; Saito, Hiromitsu; Ogawa, Tatsuhiro; Katsumata, Shigeo;
Mihara, Akira; Takahashi, Keiichi; Kobayashi, Eiji; Gomi, Katsunari
PA Kyowa Hakko Kogyo Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 05208979	A2	19930820	JP 1992-153534	19920612
PRAI JP 1991-158897		19910628		

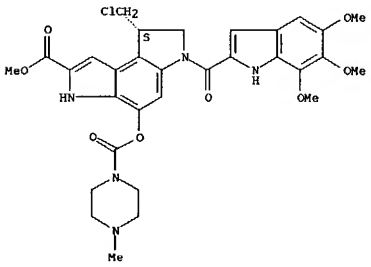
OS MARPAT 120:163825
GI



AB The title compds. I, II [R = H, CONR1R2, Q1; R1, R2 = H, lower alkyl; R3 = CH2, O, NMe; R5R6 = CH(CH2Z)CH2NX, CH2CH(CH2Z)CH2NX; X = H, Q2, Q3; X1-3 = H, OR4; X4 = NH, O; R4 = lower alkyl; Z = Cl, Br; n = 0-4; if X in I = Q3 and X4 = NH, then X1, X2, and/or X3 = H], or their salts are prepared
DC 113 in MeCN was treated with HCl at room temperature for 1 h and the reaction product was treated with p-nitrophenyl chloroformate and NEt3 in CH2Cl2 at -50° for 0.5 h followed by Me2NH at -50° to room temperature for 0.5 h to give 57% II (R = CONMe2, R5R6 = CH(CH2Cl)CH2NX, X = Q3, X1-3 =

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
OMe, X4 = NH), which inhibited growth of HeLaS3 cells with IC50 of 0.78
nM.
IT **152718-02-0P 152718-03-1P 152718-04-2P**
152718-05-3P 152718-07-5P 152718-08-6P
152718-09-7P 152718-10-0P 152718-11-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antitumor and antimicrobial agent)
RN 152718-02-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(chloromethyl)-3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

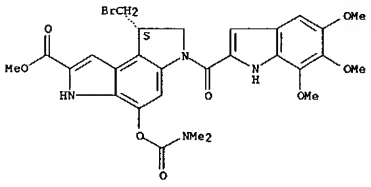
Absolute stereochemistry.



RN 152718-03-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

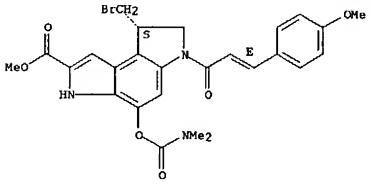
Absolute stereochemistry.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-07-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-
oxo-2-propenyl]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

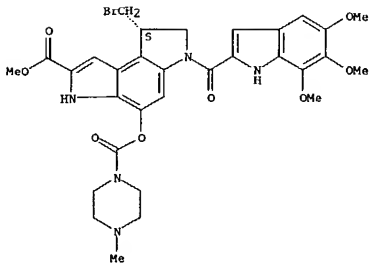
Absolute stereochemistry.
Double bond geometry as shown.



RN 152718-08-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, [S-(E)]- (9CI) (CA INDEX NAME)

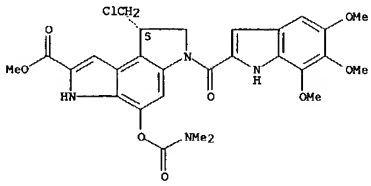
Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-04-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

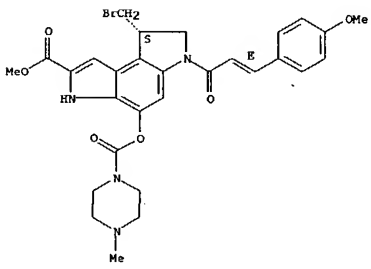
Absolute stereochemistry.



RN 152718-05-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-
[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

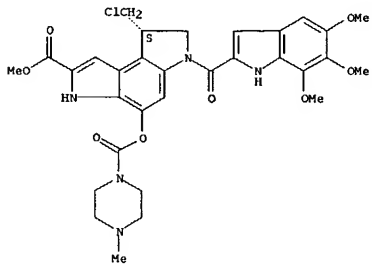
Absolute stereochemistry.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 152718-09-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid,
8-(chloromethyl)-3,6,7,8-
tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

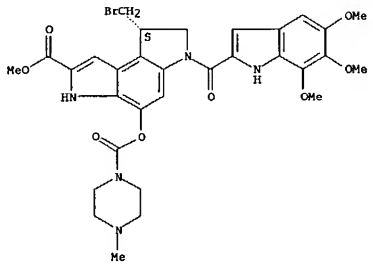
● HCl

RN 152718-10-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride, (S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

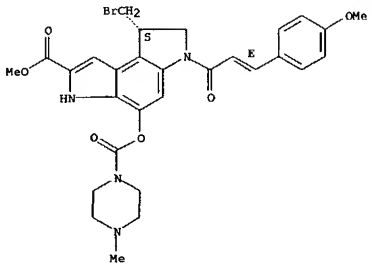
● HCl

RN 152718-11-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride, [S-(E)]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 81 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.

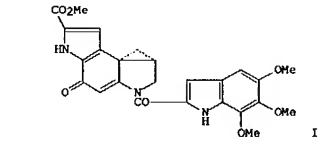
PAGE 1-A



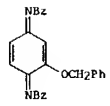
PAGE 2-A

● HCl

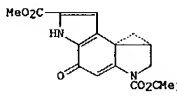
L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:649750 CAPLUS
DN 119:249750
TI Total synthesis and preliminary evaluation of (+)- and ent-(-)-duocarmycin SA
AU Boger, Dale L.; Machiya, Kozo; Hertzog, Donald L.; Kitos, Paul A.; Holmes, Daniel
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (1993), 115(20), 9025-36
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
GI



I



II



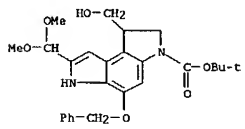
III

AB Concise total syntheses of natural (+)- (I) and ent-(-)-duocarmycin SA are based on sequential regioselective nucleophilic substitution reactions of the unsym. p-quinonediimine II in the preparation of a dihydropyrroloindole precursor to the left-hand subunit. In addition to constituting a new synthetic strategy for the preparation of I and related agents, both enantiomers of N-BOC-DSA (III) and its immediate synthetic precursors are made available by the approach. This provides access to synthetic analogs incorporating either enantiomer of the exceptionally stable and potent duocarmycin SA alkylation subunit. Studies reveal that III is 4.8 times

L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
more stable to chem. solvolysis than N-BOC-CPI, the authentic alkylation subunit of CC-1065, and that the agents participate in a stereoelectronically-controlled solvolysis reaction with nucleophilic addn. to the least hindered cyclopropane carbon. Consistent with this enhanced stability, (+)-III had the most potent inherent cytotoxic activity of all natural and synthetic alkylation subunits examd. to date including (+)-N-BOC-CPI, and its relative cytotoxic potency predictably follows a fundamental relationship between chem. stability and cytotoxic potency established in prior studies. In contrast to expectations based on past observations, the unnatural enantiomers of I and III also constituted potent cytotoxic agents whose further examn. should prove exceptionally interesting.

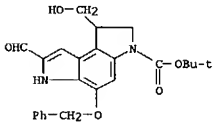
IT **144667-33-4P 144667-34-5P 144667-35-6P 144667-39-0P 144732-56-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate in preparation of duocarmycin SA)

RN 144667-33-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 7-(dimethoxymethyl)-1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

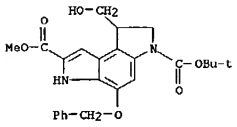


RN 144667-34-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 7-formyl-1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

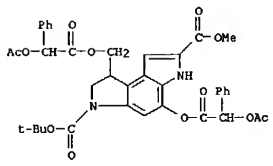


RN 144667-35-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester (9CI) (CA INDEX NAME)

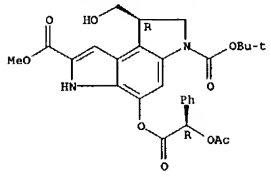


RN 144667-39-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

4-[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester, [8R-[4(R*),8R*(R*)]]- (9CI) (CA INDEX NAME)

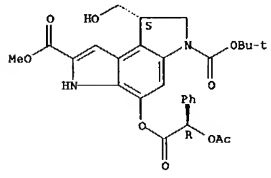


L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 150992-79-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 4-[[(acetyloxy)phenylacetyl]oxy]-7,8-dihydro-8-(hydroxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



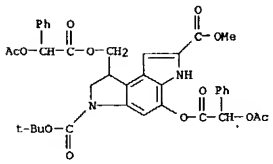
RN 150992-80-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

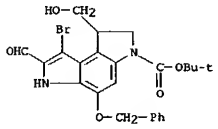
Absolute stereochemistry.

L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 144732-56-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

4-[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester, [8S-[4(S*),8R*(S*)]]- (9CI) (CA INDEX NAME)



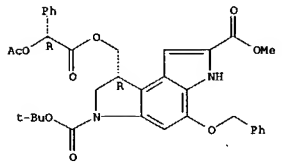
IT **150992-77-1P 150992-78-2P 150992-79-3P 150992-80-6P 150992-81-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 150992-77-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 8-bromo-7-formyl-1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 150992-78-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 4-[[(acetyloxy)phenylacetyl]oxy]-7,8-dihydro-8-(hydroxymethyl)-, 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

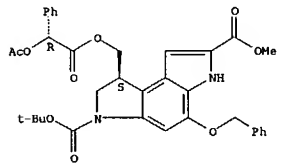
L14 ANSWER 82 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



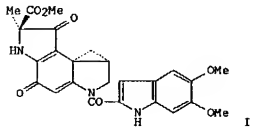
RN 150992-81-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:538951 CAPLUS
DN 119:138951
TI Synthesis and cytotoxicity of enantiomeric pairs of duocarmycin a and its
2-epimer
AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Terashima, Shiro
CS Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Nogi, 329-01, Japan
SO Bioorganic & Medicinal Chemistry Letters (1992), 2(7), 755-8
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
GI

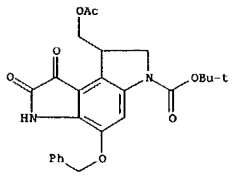


I

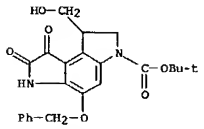
AB The synthesis of the four possible diastereomers of duocamycin A (I) was
achieved through optical resolution of a tricyclic synthetic intermediate.
The stereochem. configuration of the cyclopropane ring was found to be
closely related with their cytotoxicity against P388 murine leukemia.

IT **132628-62-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(deacetylation of)
RN 132628-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-
1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



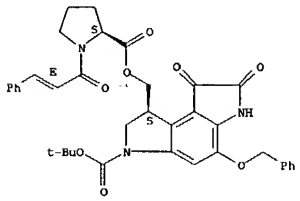
IT **143874-46-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and acylation with cinnamoylproline, and resolution of)
RN 143874-46-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-
(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)



IT **149365-69-5P 149365-70-8P 149405-53-8P**
149405-54-9P 149405-56-1P 149405-57-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to duocarmycin)
RN 149365-69-5 CAPLUS
CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)-(9CI)
(CA INDEX NAME)

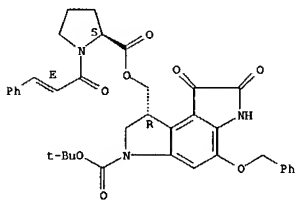
Absolute stereochemistry.
Double bond geometry as shown.

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149365-70-8 CAPLUS
CN L-Proline, 1-(1-oxo-3-phenyl-2-propenyl)-, [3-[(1,1-dimethylethoxy)carbonyl]-1,2,3,6,7,8-hexahydro-7,8-dioxo-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)-(9CI)
(CA INDEX NAME)

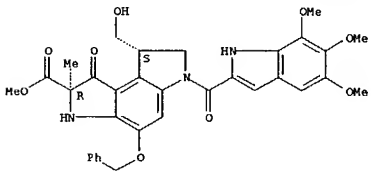
Absolute stereochemistry.
Double bond geometry as shown.



RN 149405-53-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

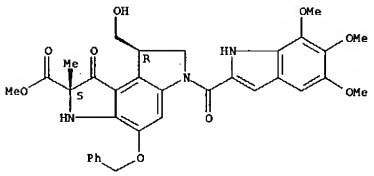
Absolute stereochemistry. Rotation (+).

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149405-54-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2S-trans)- (9CI) (CA INDEX NAME)

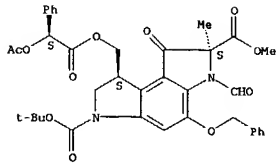
Absolute stereochemistry. Rotation (-).



RN 149405-56-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,
8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester, [2S-[2α,8α(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

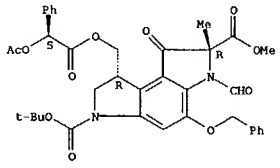
L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149405-57-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2R-[2α,8α(S*)]]- (9CI) (CA INDEX NAME)

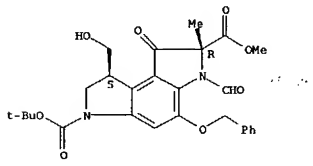
Absolute stereochemistry. Rotation (+).



IT **132628-67-2P 132628-68-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and desilylation of)
RN 132628-67-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

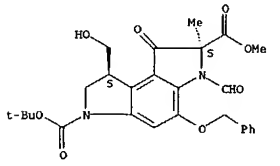
Relative stereochemistry.

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149365-67-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3,7(2H)-dicarboxylic acid, 6-formyl-1,6,7,8-tetrahydro-1-(hydroxymethyl)-7-methyl-8-oxo-5-(phenylmethoxy)-, 3-(1,1-dimethylethyl) 7-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

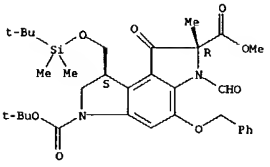


IT **149365-68-4P 149405-52-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation, hydrolysis, and acylation of, with indolylcarboxylate)
RN 149365-68-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester,
[2R-[2α,8β(S*)]]- (9CI) (CA INDEX NAME)

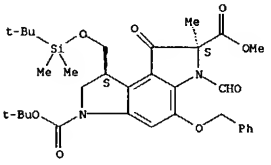
Absolute stereochemistry. Rotation (+).

L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-68-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

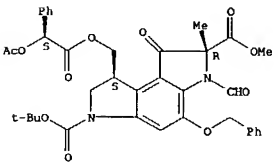
Relative stereochemistry.



IT **149365-66-2P 149365-67-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation, acylation, and resolution of)
RN 149365-66-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 3-formyl-2,3,7,8-tetrahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

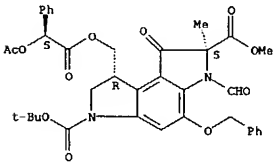
L14 ANSWER 83 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 149405-52-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid,

8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 2-methyl 6-(1,1-dimethylethyl) ester,
[2S-[2α,8β(R*)]]- (9CI) (CA INDEX NAME)

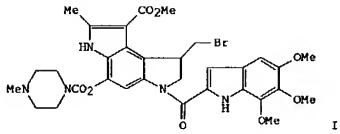
Absolute stereochemistry. Rotation (-).



L14 ANSWER 84 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:456138 CAPLUS
DN 119:56138
TI Hydrobromide of antitumor DC-89 with high stability
IN Nagamura, Satoru; Saito, Hiromitsu; Hayakawa, Eiji; Kato, Yasuki; Naganuma, Hirotake
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 537575	A1	19930421	EP 1992-116898	19921002
	R: DE, FR, GB, IT				
	JP 05097853	A2	19930420	JP 1991-259188	19911007
	CA 2079733	AA	19930408	CA 1992-2079733	19921002
PRAI	JP 1991-259188		19911007		

GI



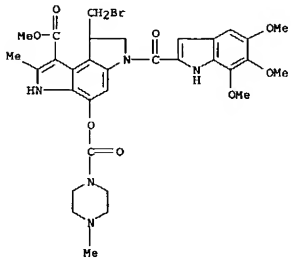
I

AB Hydrobromide of antitumor DC-89 (I) with high stability in solns. for producing freeze-dried prepns. are prepared by reaction of HBr with the base. The residual rate of a solution of 1 mg I/mL at 25° after 6 h was 98 %. Antitumor activity of I against sarcoma tumor was equal to its HCl salt.

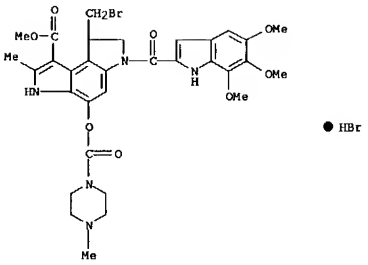
IT **148778-32-9P**
RL: PREP (Preparation)
(preparation of, with high stability in solns.)

RN 148778-32-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrobromide (9CI) (CA INDEX NAME)

L14 ANSWER 84 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 84 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



● HBr

IT **134106-78-8**
RL: PROC (Process)
(salt formation of, with hydrobromic acid, with high stability in solns.)

RN 134106-78-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:191718 CAPLUS
DN 118:191718
TI Preparation of DC-89 derivatives as neoplasm inhibitors and antibacterials
IN Nagamura, Satoru; Saito, Hiromitsu; Kobayashi, Eiji; Gomi, Katsushige
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 520435	A2	19921230	EP 1992-110688	19920625
	EP 520435	A3	19930505		
	R: DE, FR, GB, IT				
	JP 05178858	A2	19930720	JP 1992-167102	19920625
	US 5258383	A	19931102	US 1992-903756	19920625
PRAI	JP 1991-158896		19910628		

OS MARPAT 118:191718
GI

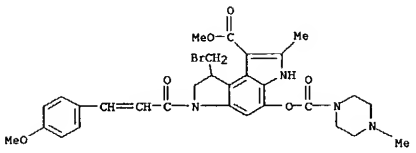
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. (I: X = H, CO2Me; Q = Q1, Q2; W = H, Q3; W1, W2 = H, OR4; R4 = alkyl, alkenyl; Z = Cl, Br; R = H, carbamoyl), were prepared Thus, precursor II was N-deacylated with NaOMe in MeOH (99% yield) and the product was condensed with 4-nitrophenyl 4-methoxycinnanate using NaH in DMF (85% yield). The cinnamide was stirred with 48% HBr in MeCN to give a residue which in CH2Cl2 was treated sequentially p-nitrophenyl chloroformate, Et3N, and aq- Me2NH to give 90% title compound III. III at 8.0 mg/kg i.v. in mice implanted with sarcoma 180 tumors reduced tumor volume to 2-7% of the volume of untreated controls.

IT **146910-07-8P 146910-08-9P 146910-09-0P**
146940-70-7P 146940-71-8P 146940-72-9P
146940-73-0P 146940-74-1P 146940-75-2P
146940-76-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor)

RN 146910-07-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-, methyl ester, monohydrochloride (9CI) (CA

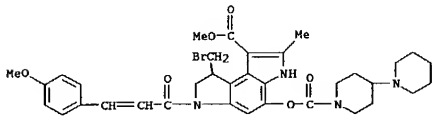
L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)



● HCl

RN 146910-08-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[{[1,4'-bipiperidin]-1'-

ylcarbonyl)oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-
1-oxo-2-propenyl]-2-methyl-, methyl ester, monohydrochloride (9CI)
(CA
INDEX NAME)

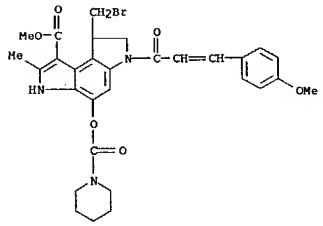


● HCl

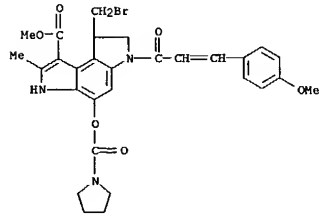
RN 146910-09-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-[2-[(1
-
methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl
ester,

L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



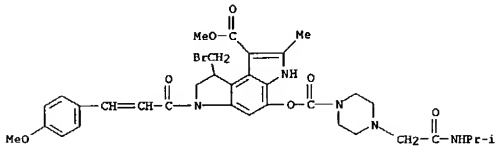
RN 146940-72-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(1-
pyrrolidinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 146940-73-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl
-
1-piperazinyl)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

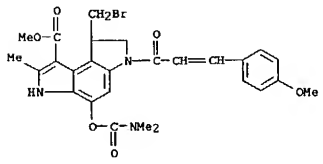
L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
monohydrochloride (9CI) (CA INDEX NAME)



● HCl

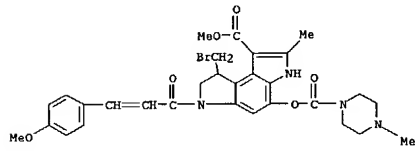
RN 146940-70-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-

[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-
oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



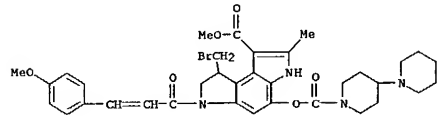
RN 146940-71-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-
tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[(1-
piperidinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



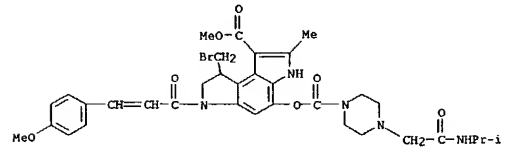
RN 146940-74-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
4-[{[1,4'-bipiperidin]-1'-

ylcarbonyl)oxy]-8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-
1-oxo-2-propenyl]-2-methyl-, methyl ester (9CI) (CA INDEX NAME)



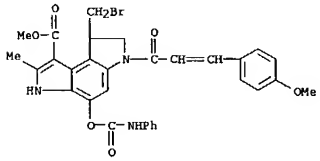
RN 146940-75-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid,
8-(bromomethyl)-3,6,7,8-

tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[[4-[2-[(1-
methylethyl)amino]-2-oxoethyl]-1-piperazinyl]carbonyl]oxy]-, methyl
ester
(9CI) (CA INDEX NAME)



RN 146940-76-3 CAPLUS

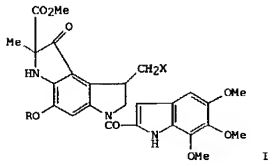
L14 ANSWER 85 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-tetrahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(phenylamino)carbonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:38908 CAPLUS
DN 118:38908
TI Preparation of DC-89 derivatives
IN Saito, Hiromitsu; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

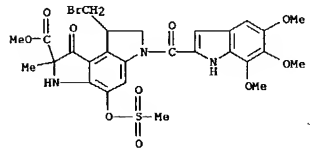
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 499130	A1	19920819	EP 1992-101913	19920205
	R: DE, FR, GB, IT				
	JP 05051384	A2	19930302	JP 1992-20059	19920205
PRAI	JP 1991-21243		19910215		

OS MARPAT 118:38908
GI

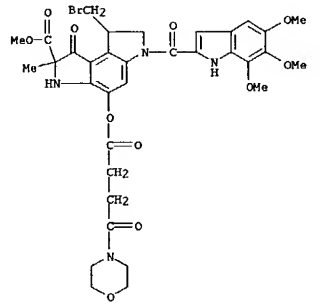


AB Title compds. I (X = Br, Cl; R = R1O2S, CO(CH2)nR2, wherein R1 = C1-6 alkyl, Ph, R2 = substituted heterocyclyl, n = 0-5) or a salt thereof, useful as antitumor agents, are prepared To DC-89B2 in CH2C12 was added DCC in CH2C12 followed by 3-(4-morpholinocarbonyl)propionic acid in CH2C12 to give I (X = Br, R = 4-morpholino-1-oxobutanoyl) (II). The IC50 of II on growth inhibitory effect against HeLaS3 cells was 0.054 nM.
IT **144258-83-3P 144258-84-4P 144258-85-5P**
144258-86-6P 144258-87-7P 144258-88-8P
144258-89-9P 144258-90-2P 144258-91-3P
144258-92-4P 144258-93-5P 144258-94-6P
144773-23-9P 144773-24-0P 144773-25-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antitumor agent)
RN 144258-83-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

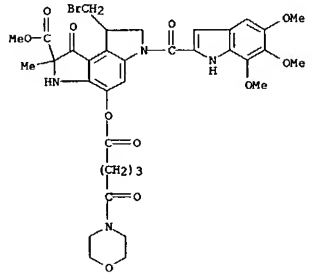


RN 144258-84-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1,4-dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



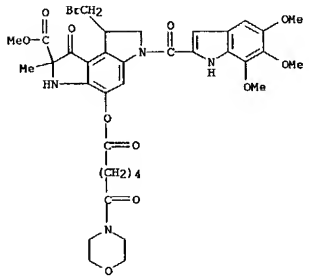
L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 144258-85-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1,5-dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 144258-86-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[6-(4-morpholinyl)-1,6-dioxohexyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

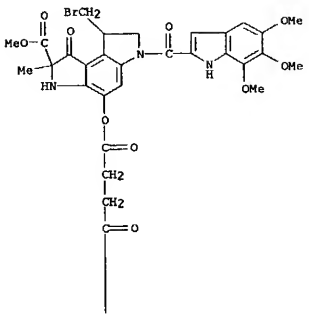
L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



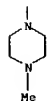
RN 144258-87-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-methyl-1-piperazinyl)-1,4-dioxobutoxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

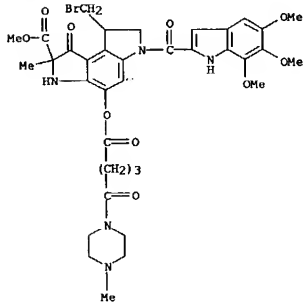


PAGE 2-A

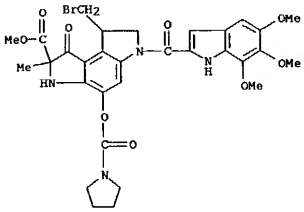


RN 144258-88-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-methyl-1-piperazinyl)-1,5-dioxopentyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

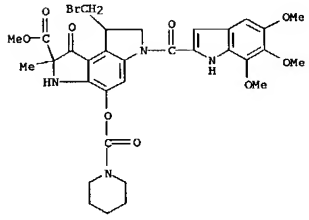


RN 144258-89-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

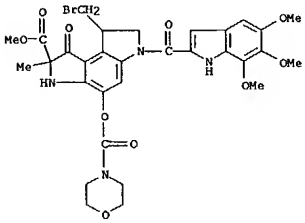


RN 144258-90-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
NAME)

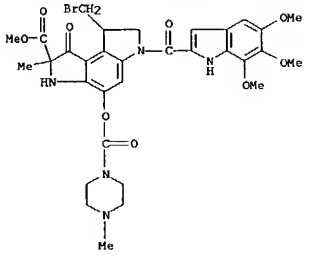


RN 144258-91-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[(4-morpholinylcarbonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

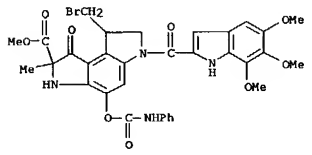


RN 144258-92-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

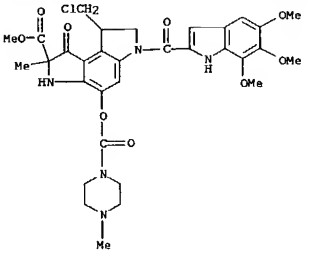


RN 144258-93-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[(phenylamino)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

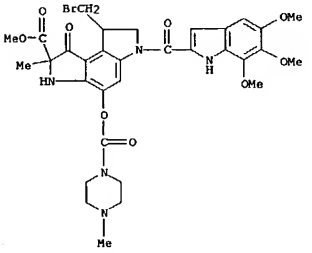


RN 144258-94-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

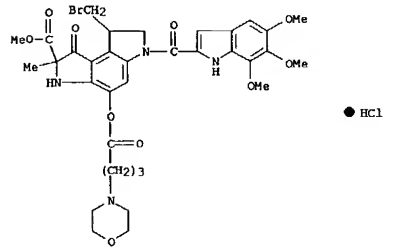
L14 ANSWER 86 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



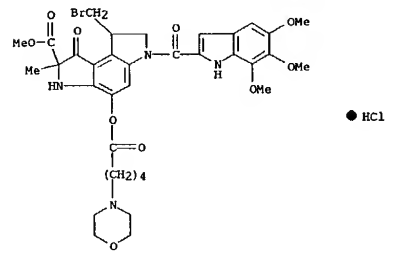
RN 144773-23-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



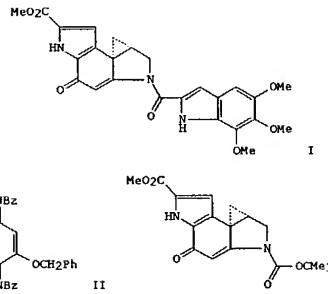
RN 144773-24-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[4-(4-morpholinyl)-1-oxobutoxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



RN 144773-25-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-4-[[5-(4-morpholinyl)-1-oxopentyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)



L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:38646 CAPLUS
DN 118:38646
TI Total synthesis of (+)-duocarmycin SA
AU Boger, Dale L.; Machiya, Kozo
CS Dep. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Journal of the American Chemical Society (1992), 114(25), 10056-8
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 118:38646
GI

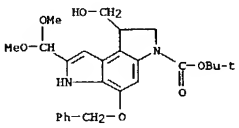


I

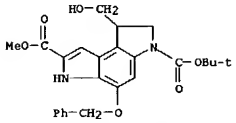
II III

AB A concise total synthesis of natural (+)-duocarmycin SA (I) is based on sequential regioselective nucleophilic substitutition reactions of the unsym. p-quinone diimide II leading to a dihydropyrroloindole precursor to the left-hand subunit. In addition to constituting a new synthetic strategy for the preparation of agents related to the natural or synthetic members of the duocarmycin class of antitumor-antibiotics, both enantiomers of N-BOC DSA (III) and its immediate synthetic precursors are now available. This provides access to synthetic analogs incorporating either enantiomer of the exceptionally stable and potent duocarmycin SA alkylation subunit.
IT **144667-33-4P**

L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and acetal hydrolysis of)
RN 144667-33-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 7-(dimethoxymethyl)-
1,6-dihydro-1-(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester
(9CI) (CA INDEX NAME)

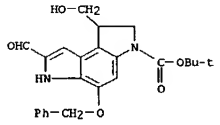


IT **144667-35-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenolysis of)
RN 144667-35-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid, 7,8-dihydro-8-(hydroxymethyl)-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl)
2-methyl ester (9CI) (CA INDEX NAME)



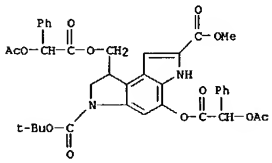
IT **144667-39-0P 144732-56-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrolysis of)
RN 144667-39-0 CAPLUS

L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)



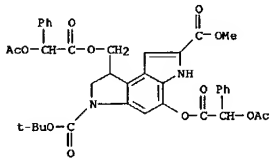
L14 ANSWER 87 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

4-[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester,
[8R-[4(R*),8R*(R*)]]-
(9CI) (CA INDEX NAME)



RN 144732-56-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(3H)-dicarboxylic acid,

4-[[(acetyloxy)phenylacetyl]oxy]-8-[[[(acetyloxy)phenylacetyl]oxy]methyl]-7,8-dihydro-, 6-(1,1-dimethylethyl) 2-methyl ester,
[8S-[4(S*),8R*(S*)]]-
(9CI) (CA INDEX NAME)

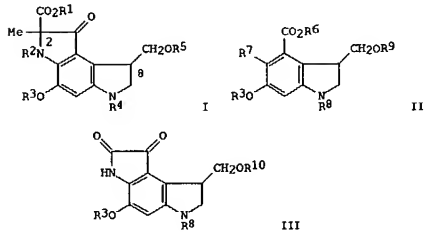


IT **144667-34-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and oxidation of)
RN 144667-34-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 7-formyl-1,6-dihydro-1-
(hydroxymethyl)-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:591827 CAPLUS
DN 117:191827
TI Preparation of 2-alkoxycarbonyl-2-methyl-1-oxo-1,2,3,6,7,8-hexahydrobenzo[1,2-b;4,3-b']dipyrrole derivatives as intermediates for duocarmycins
IN Terajima, Atsuro; Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio
PA Sagami Chemical Research Center, Japan
SO Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 04117383	A2	19920417	JP 1990-159828	19900620
JP 3037965	B2	20000508		
PRAI JP 1990-159828		19900620		

OS MARPAT 117:191827
GI

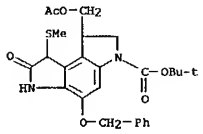


AB The title compds. (I; R1 = H, C1-6 linear or branched alkyl; R2, R4 = H,
amino-protecting group; R3, R5 = H, hydroxy-protecting group) and their
intermediates [II and III: R3, R9, R10 = H, hydroxy-protecting group; R6 =
H, C1-6 linear or branched alkyl; R7 = (un)substituted amino; R8 = H,
amino-protecting group] are prepared I are useful as intermediates for the
anticancer agents duocarmycin A, B1, C1 (pyrindamycin B), and C2
(pyrindamycin A). Thus, oxidation of III (R3 = PhCH2, R8 = CO2CMe3, R10 =
SiMe2CMe3) (preparation given) with m-ClC6H4CO2OH in CH2Cl2 and methanolysis of
the resulting isatoic acid anhydride derivative in the presence of K2CO3 gave

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
II (R3 = PhCH2, R6 = Me, R7 = H2N, R8 = CO2CMe3, R9 = SiMe2CMe3). Alkylation of this with BrCHMeCO2Me in the presence of Cs2CO3 in DMF and formylation of the resultant II (R7 = NHCHMeCO2Me; R3, R6-R9 = same as above) gave II [R7 = N(CHO)CHMeCO2Me; R3, R6-R9 = same as above], which was cyclized by treatment with (Me2CH)2NLi in THF at -78° for 5.5 h to give (2R*,8S*)- and (2S*,8S*)-I (R1 = Me, R2 = CHO, R3 = PhCH2, R4 = CO2CMe3, R5 = SiMe2CMe3). These were converted into dl-duocarmycin A or -epiduocarmycin A.

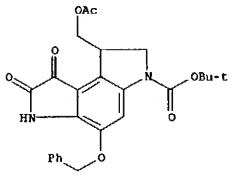
IT **132628-61-6P 132628-62-7P 132628-63-8P 132628-67-2P 132628-68-3P 132628-70-7P 132628-71-8P 143314-86-7P 143874-46-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for duocarmycins or pyrindamycins)

RN 132628-61-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-8-(methylthio)-7-oxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

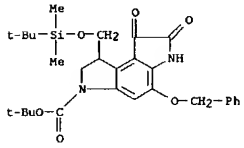


RN 132628-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



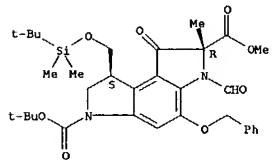
RN 132628-63-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 132628-67-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

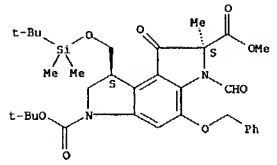
Relative stereochemistry.

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-68-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

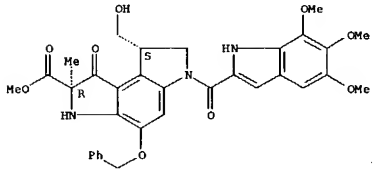
Relative stereochemistry.



RN 132628-70-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

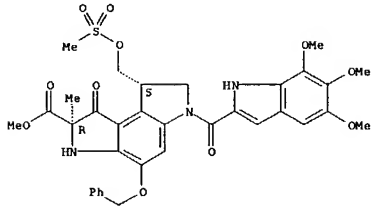
Relative stereochemistry.

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-71-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

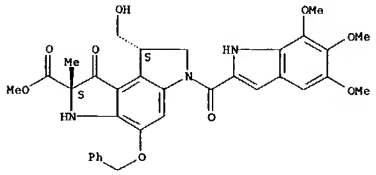
Relative stereochemistry.



RN 143314-86-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

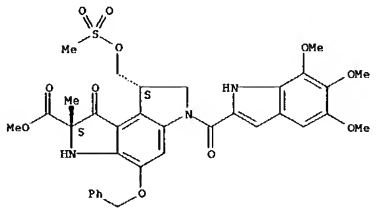
L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 143314-87-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

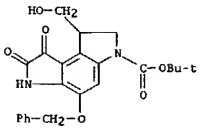
methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 143874-46-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 88 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1992:591589 CAPLUS

DN 117:191589

TI Preparation of 2-epiduocarmycin A as antitumor agent

IN Terajima, Atsuro; Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio

PA Zaidan Hojin Sagami Chuo Kagaku Kenkyusho, Japan

SO Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF

DT Patent

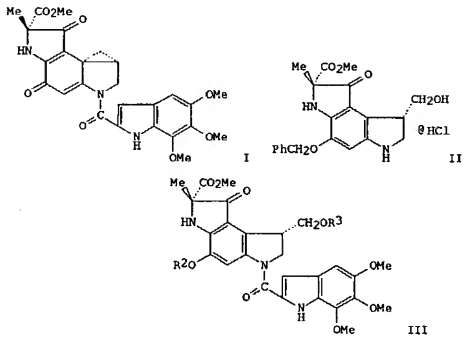
LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 04099774	A2	19920331	JP 1990-213741	19900814
PRAI JP 1990-213741		19900814		

OS MARPAT 117:191589

GI



AB 2-Epiduocarmycin A (I) and its intermediates are prepared Condensation of (2S,8S)-II with 6,7,8-trimethoxy-1H-indole-2-carboxylic acid and 1-(3-dimethylaminopropyl)ethylcarbodiimide HCl in DMF gave 62% indolyl derivative (2S,8S)-III (R2 = PhCH2, R3 = H), which was mesylated with MeSO2Cl in CH2Cl2 to give 99% mesylate (2S,8S)-III (R2 = PhCH2, R3 = MeSO2) (IV).

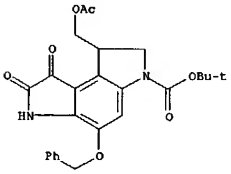
L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Hydrogenolysis of IV over 10% Pd-C gave 83% phenolic deriv. (2S,8S)-III (R2 = H, R3 = MeSO2), which was treated with NaH (50% oil dispersion) in THF with stirring at room temp. to give 56% (DL)-I, which showed IC50 of 1.7 + 10-4 μg/mL against P-388 leukemic cells.

IT **132628-62-7P 132628-63-8P 132628-67-2P**
132628-68-3P 132628-70-7P 132628-71-8P
143314-86-7P 143314-87-8P 143874-46-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antitumor agent)

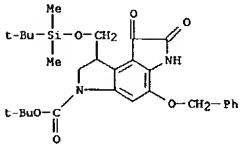
RN 132628-62-7 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 132628-63-8 CAPLUS

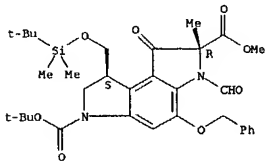
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 132628-67-2 CAPLUS

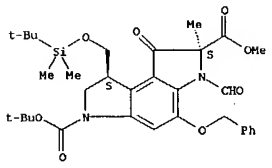
L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 132628-68-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

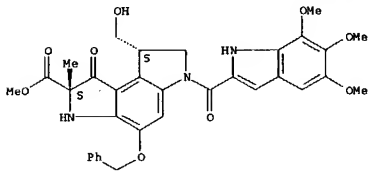


RN 132628-70-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

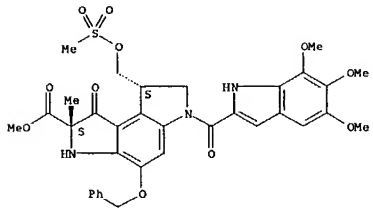
L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 143314-87-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

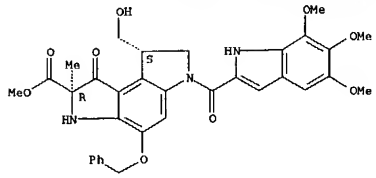
methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 143874-46-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6,7,8-tetrahydro-1-(hydroxymethyl)-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

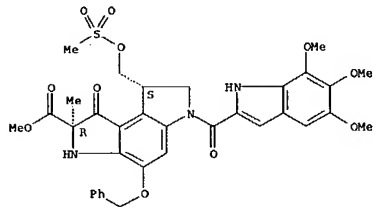
L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 132628-71-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

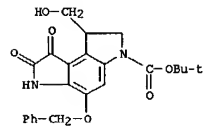


RN 143314-86-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

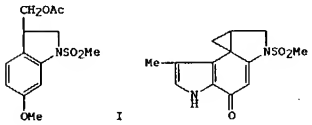
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L14 ANSWER 89 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

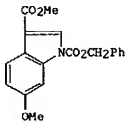


L14 ANSWER 90 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:194003 CAPLUS
DN 116:194003
TI Tandem Michael addition-[3,3]sigmatropic rearrangement processes. Part 2. Construction of cyclopropa[3,4]pyrrolo[3,2-e]indol-4-one (CPI) unit of antitumor antibiotic CC-1065
AU Toyota, Masahiro; Fukumoto, Keiichiro
CS Pharm. Inst., Tohoku Univ., Sendai, 980, Japan
SO Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1992), (5), 547-52
CODEN: JCPRB4; ISSN: 0300-922X
DT Journal
LA English
GI



I

II

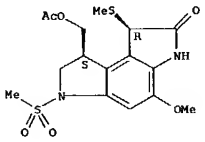


III

AB Development of an alternative strategy for preparing 3-acetoxymethyl-2,3-dihydro-1-methylsulfonyl-6-methoxyindole (I) has been completed. Since I was an intermediate in a previous synthesis of the CPI unit (II) of CC-1065, this achievement constitutes a formal synthesis of racemic II. The key strategic element of the approach involves the tandem Michael addition-[3,3]sigmatropic rearrangement process of HC.tplbond.CCO2Me and 3-MeOC6H4N(OH)CO2CH2Ph, prepared from 3-O2NC6H4OMe, to furnish indole III as the sole product. Subsequent elaboration of III into I was then achieved

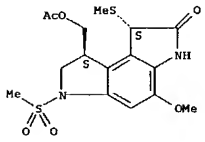
L14 ANSWER 90 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
by applying M. P. Cava et al's (1989) technique. The conversion of I into II was also achieved with the method of W. Wierenga (1981).
IT **140862-50-6P 140862-51-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)
RN 140862-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 140862-51-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, trans- (9CI) (CA INDEX NAME)

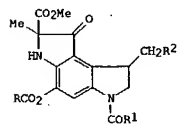
Relative stereochemistry.



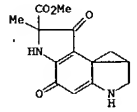
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:106269 CAPLUS
DN 116:106269
TI Preparation of DC-89 derivatives as neoplasm inhibitors
IN Saito, Hiromitsu; Asai, Akira; Nagamura, Satoru; Kobayashi, Eiji; Gomi, Katsushige
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 461603	A1	19911218	EP 1991-109533	19910611
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 5214065	A	19930525	US 1991-710407	19910605
	JP 04226988	A2	19920817	JP 1991-137741	19910610
	US 5248692	A	19930928	US 1993-24472	19930301
PRAI	JP 1990-152098		19900611		
	US 1991-710407		19910605		

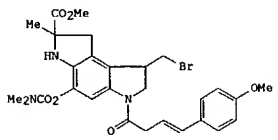
OS MARPAT 116:106269
GI



I



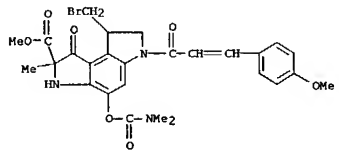
II



III

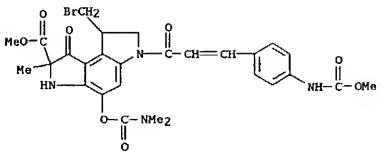
AB Title compds. [I; R = amino, morpholino, pyrrolidinyl, piperidinyl, homopiperidinyl, etc.; R1 = (substituted) phenylethenyl, phenoxymethyl, acylaminoindolyl; etc.; R2 = Cl, Br], were prepared Thus, antibiotic DC-88A was stirred with NaOMe in MeOH to give 97% intermediate II. II was acylated with p-nitrophenyl 4-methoxycinnamate/NaH and the product was

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
treated with aq. HBr and then Me2NCOCl to give title compd. III. III at 16 mg/kg i.v. in mice reduced the size of sarcoma 180 tumors to 7.8% of controls.
IT **139147-43-6P 139147-44-7P 139147-45-8P**
139147-46-9P 139147-47-0P 139147-48-1P
139147-49-2P 139147-50-5P 139147-51-6P
139147-52-7P 139147-53-8P 139147-54-9P
139147-55-0P 139147-56-1P 139147-57-2P
139147-58-3P 139147-59-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as neoplasm inhibitor)
RN 139147-43-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

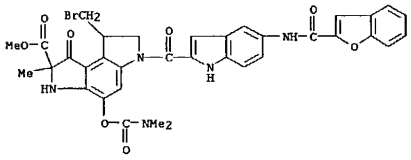


RN 139147-44-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-[4-[(methoxycarbonyl)amino]phenyl]-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

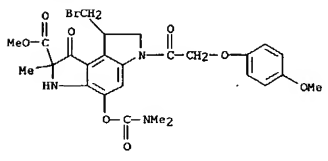


RN 139147-45-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

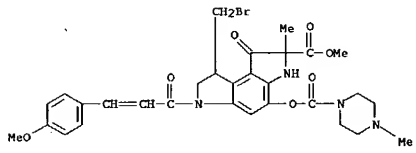


RN 139147-46-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-6-[5-(3,4-dimethoxyphenyl)-1-oxo-2,4-pentadienyl]-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

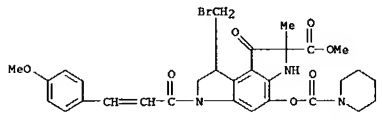
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 139147-49-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

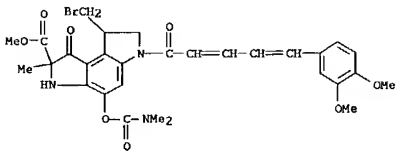


RN 139147-50-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-4-[(1-piperidinylcarbonyl)oxy]-, methyl ester (9CI) (CA INDEX NAME)

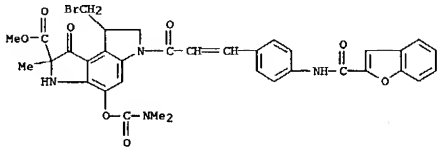


RN 139147-51-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



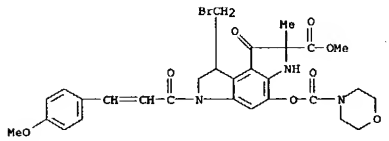
RN 139147-47-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-[4-[(2-benzofuranylcarbonyl)amino]phenyl]-1-oxo-2-propenyl]-8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



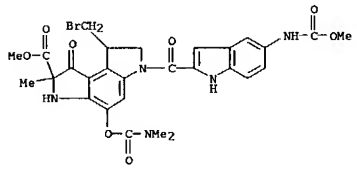
RN 139147-48-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(4-methoxyphenoxy)acetyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

[(4-morpholinylcarbonyl)oxy]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

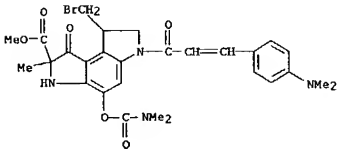


RN 139147-52-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[[5-[(methoxycarbonyl)amino]-1H-indol-2-yl]carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

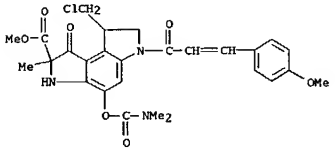


RN 139147-53-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

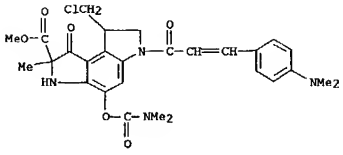


RN 139147-54-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

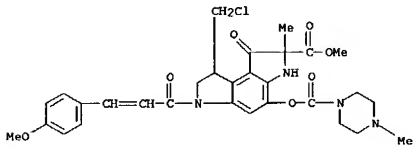


RN 139147-55-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-4-[[(dimethylamino)carbonyl]oxy]-6-[3-[4-(dimethylamino)phenyl]-1-oxo-2-propenyl]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

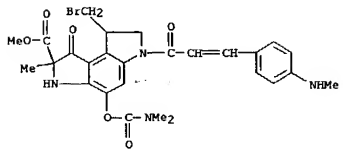


RN 139147-56-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(chloromethyl)-1,2,3,6,7,8-hexahydro-6-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

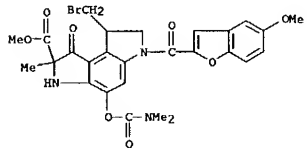


RN 139147-57-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[3-[4-(methylamino)phenyl]-1-oxo-2-propenyl]-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

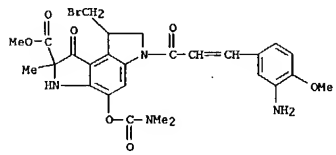
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 139147-58-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-6-[(5-methoxy-2-benzofuranyl)carbonyl]-2-methyl-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 139147-59-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 6-[3-(3-amino-4-methoxyphenyl)-1-oxo-2-propenyl]-8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo- (9CI) (CA INDEX NAME)

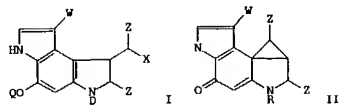


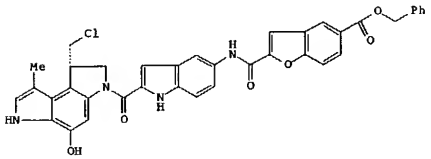
L14 ANSWER 91 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:83450 CAPLUS
DN 116:83450
TI Preparation of CC-1065 analogs as neoplasm inhibitors.
IN Aristoff, Paul Adrian; Kelly, Robert Charles; Mitchell, Mark Allen
PA Upjohn Co., USA
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9116324	A1	19911031	WO 1991-US2704	19910424
	W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
	CA 2078118	AA	19911026	CA 1991-2078118	19910424
	CA 2078118	C	19991116		
	AU 9177954	A1	19911111	AU 1991-77954	19910424
	AU 648313	B2	19940421		
	EP 527189	A1	19930217	EP 1991-909127	19910424
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05508394	T2	19931125	JP 1991-508837	19910424
	US 5739350	A	19980414	US 1995-479231	19950607
PRAI	US 1990-513501	A2	19900425		
	WO 1991-US2704	A	19910424		
	US 1992-966139	B1	19921023		
	US 1994-279767	B1	19940725		

OS MARPAT 116:83450
GI





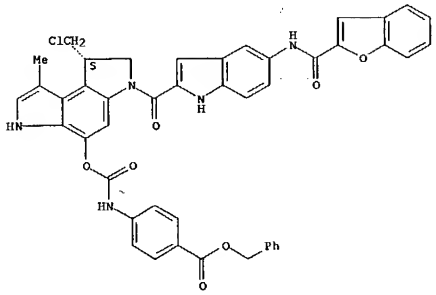
III

AB Title compds. [I and II; W, Z = H, alkyl, Ph; X = halo, N3, (thio)cyanate, (thio)isocyanate, phosphate ester, sulfonyl, etc.; D, R = heteroarylacyl; Q = H, (thio)acyl, alkoxy or phenoxycarbonyl, (thio)carbamoyl, etc.], were prepared as synthetic intermediates and as neoplasm inhibitors. They may also be linked to monoclonal antibodies or human CD4 protein. Thus, title compound III was prepared from 1,1-dimethylethyl S-1-chloromethyl-1,6-dihydro-5-hydroxy-8-methylbenzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylate and the corresponding benzimidazolecarboxylic acid derivative (preparation given) via deprotection of the benzodipyrrole and carbodiimide coupling. Title compds. at 0.1-0.4 mg/kg showed T/C = 133-200% against <1210 leukemia in mice.

IT **138730-88-8P 138730-91-3P 138730-94-6P 138731-06-3P 138731-08-5P 138731-09-6P 138731-11-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as neoplasm inhibitor and intermediate)

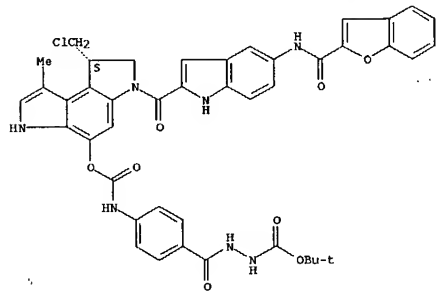
RN 138730-88-8 CAPLUS
CN Benzoic acid, 4-[[[[3-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrol-5-yl]oxy]carbonyl]amino]-, phenylmethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 138730-91-3 CAPLUS
CN Hydrazinecarboxylic acid, 2-[4-[[[[3-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrol-5-yl]oxy]carbonyl]amino]benzoyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

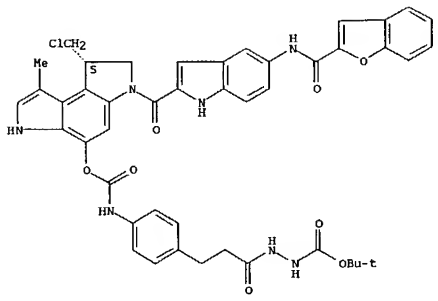
Absolute stereochemistry.



RN 138730-94-6 CAPLUS
CN Hydrazinecarboxylic acid, 2-[3-[4-[[[[3-[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]-1-(chloromethyl)-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrol-5-yl]oxy]carbonyl]amino]phenyl]-1-oxopropyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

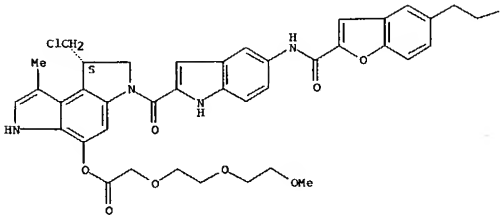


RN 138731-06-3 CAPLUS
CN Hydrazinecarboxylic acid, 2-[3-[2-[[[2-[[1-(chloromethyl)-1,6-dihydro-5-[[[2-(2-methoxyethoxy)ethoxy]acetyl]oxy]-8-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-5-benzofuranyl]-1-oxopropyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

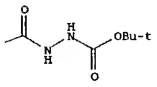
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

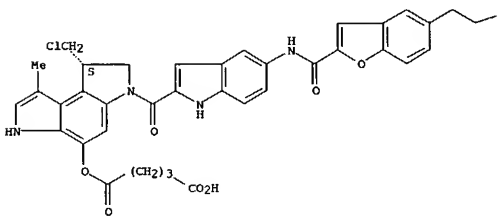


RN 138731-08-5 CAPLUS
CN Pentanedioic acid, mono[1-(chloromethyl)-3-[[5-[[[5-[3-[2-[(1,1-dimethylethoxy)carbonyl]hydrazino]-3-oxopropyl]-2-benzofuranyl]carbonyl]amino]-1H-indol-2-yl]carbonyl]-1,2,3,6-tetrahydro-8-methylbenzo[1,2-b:4,3-b']dipyrrol-5-yl] ester, (S)- (9CI) (CA INDEX NAME)

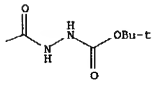
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

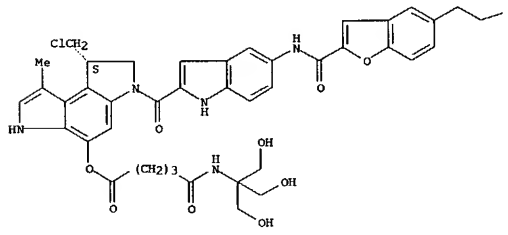


RN 138731-09-6 CAPLUS
CN Hydrazinecarboxylic acid, 2-[3-[2-[[[2-[[1-(chloromethyl)-1,6-dihydro-5-[[5-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]-1,5-dioxopentyl]oxy]-8-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-5-benzofuranyl]-1-oxopropyl]-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

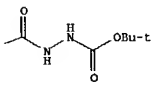
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

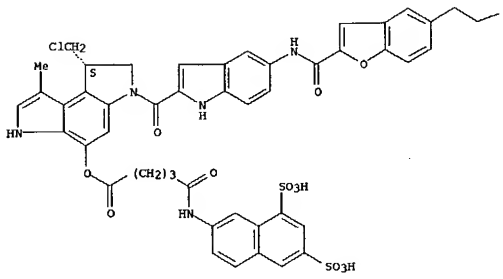


RN 138731-11-0 CAPLUS
CN Hydrazinecarboxylic acid, 2-[3-[2-[[[2-[[1-(chloromethyl)-5-[[5-[(6,8-disulfo-2-naphthalenyl)amino]-1,5-dioxopentyl]oxy]-1,6-dihydro-8-methylbenzo[1,2-b:4,3-b']dipyrrol-3(2H)-yl]carbonyl]-1H-indol-5-yl]amino]carbonyl]-5-benzofuranyl]oxopropyl]-, 1,1-dimethylethyl ester, disodium salt, (S)- (9CI) (CA INDEX NAME)

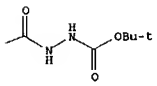
Absolute stereochemistry.

L14 ANSWER 92 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



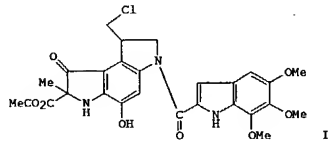
●2 Na

L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

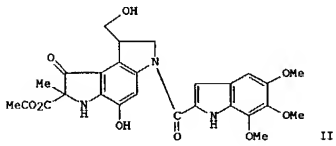
AN 1992:19720 CAPLUS
DN 116:19720
TI Antibiotics SF2582 manufacture with Streptomyces
IN Ohba, Kazunori; Watabe, Hiroomi; Nagasawa, Mieko; Sakakibara, Shiro; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi; Koyama, Masao; Nakazawa, Tadashi; Yamamoto, Haruo
PA Meiji Seika Kaisha, Ltd., Japan
SO U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 276,714, abandoned. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4994578	A	19910219	US 1989-344738	19890428
	JP 01139590	A2	19890601	JP 1987-297476	19871127
	JP 01265890	A2	19891023	JP 1988-94544	19880419
	JP 01275581	A2	19891106	JP 1988-103782	19880428
	JP 2562935	B2	19961211		
	US 5037993	A	19910806	US 1990-520424	19900508
PRAI	JP 1987-297476		19871127		
	JP 1988-94544		19880419		
	JP 1988-103782		19880428		
	US 1988-276714		19881128		
	US 1989-344738		19890428		

GI



I



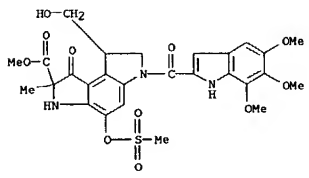
II

L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB The antibiotics SF2582 A (I), B, and C (II), also useful as neoplasm inhibitors, are manufactured by culture of Streptomyces. Derivs. of the antibiotics having improved antitumor activities are prepared Streptomyces SF2582 was shake-cultured for 5 days at 28°, and the cell mass from 1000 L culture broth recovered by filtration. I, antibiotic SF2582B, and II 182, 88, and 450 mg, resp., were recovered from the cell mass by extraction and chromatog. The sulfate or alkyl- or arylsulfonate derivs. (4) were prepared from II and their antitumor activity determined Against P388 cells, the derivs. had LC50 (ng/mL) of 4-2500, as compared to 9400 for II. Also given was the morphol. and physiol. characteristics of Streptomyces SF2582. The physicochem. characteristics of I, SF2582B, and II were also given.

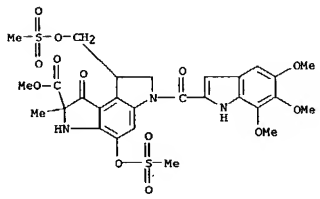
IT **126590-90-7P 136483-61-9P 136483-62-0P 136772-69-5P**
RL: PREP (Preparation)
(preparation of, from antibiotic SF2582C, enhanced antitumor activity of)

RN 126590-90-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

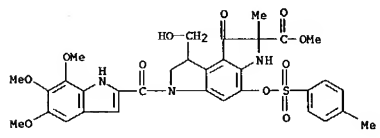


RN 136483-61-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-methyl-4-[(methylsulfonyl)oxy]-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

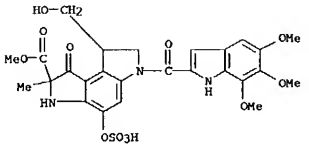


RN 136483-62-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[[(4-methylphenyl)sulfonyl]oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 136772-69-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-1-oxo-4-(sulfooxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 93 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1991:408427 CAPLUS

DN 115:8427

TI Preparation of DC-88A derivatives as antitumor agents

IN Kanda, Yutaka; Uosaki, Youichi; Saito, Hiromitsu; Sano, Hiroshi; Kobayashi, Eiji; Morimoto, Makoto; Nagamura, Satoru

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW

DT Patent

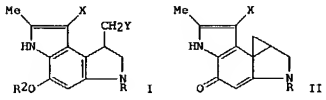
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 406749	A1	19910109	EP 1990-112563	19900702
	EP 406749	B1	19991027		
	R: DE, FR, GB, IT				
	JP 03128379	A2	19910531	JP 1990-168666	19900627
	JP 2510335	B2	19960626		
	US 5070092	A	19911203	US 1990-545579	19900629
	US 5187186	A	19930216	US 1991-755760	19910906
PRAI	JP 1989-171605		19890703		
	US 1990-545579		19900629		

OS MARPAT 115:8427

GI



AB The title compds. (I and II; R = 5,6,7-trimethoxy-2-indolylcarbonyl; R2 = H, alkanoyl, dialkylcarbamoyl, alkoxycarbonyl, trialkylsilyl, etc.; X = H, CO2R1; R1 = H, alkyl, allyl, PhCH2; Y = Cl, Br) were prepared Thus, DC89B2 (fermentation preparation given) was converted in 3 steps to I (R2 = SiMe2CMe3, X = CO2Me, Y = Br) which suppressed Sarcoma 180 tumor growth in mice to 4.3 volume% that of controls 7 days after administration of 0.25 mg/kg i.v.

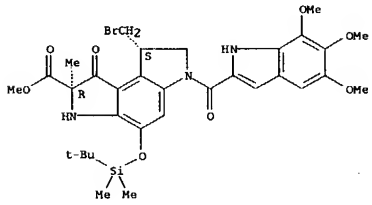
IT **129953-15-7P 134106-83-5P 134106-84-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(prepn. and reaction of, in prepn. of antitumor agents)

RN 129953-15-7 CAPLUS

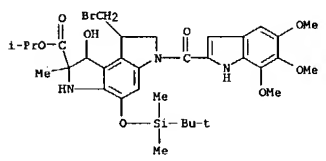
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 134106-83-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

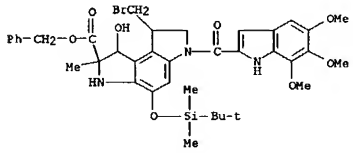


RN 134106-84-6 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

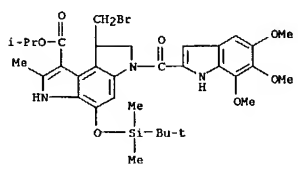
6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT **134106-73-3P 134106-75-5P 134106-76-6P**
134106-77-7P 134106-78-8P 134106-79-9P
134106-80-2P 134106-81-3P 134106-82-4P
134127-18-7P 134127-20-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antitumor agent)

RN 134106-73-3 CAPLUS

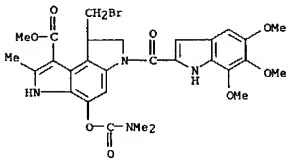
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



RN 134106-75-5 CAPLUS

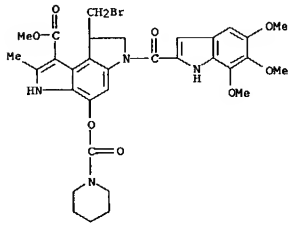
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-76-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

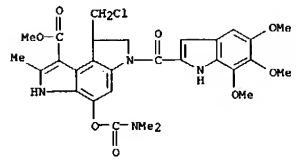
tetrahydro-2-methyl-4-[(1-piperidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134106-77-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

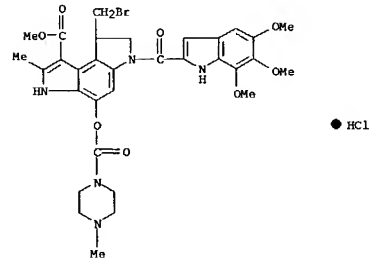
tetrahydro-2-methyl-4-[(1-pyrrolidinylcarbonyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-80-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

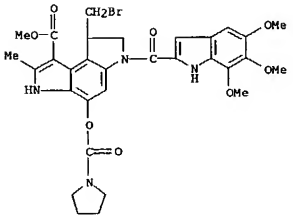
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI)
(CA INDEX NAME)



RN 134106-81-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

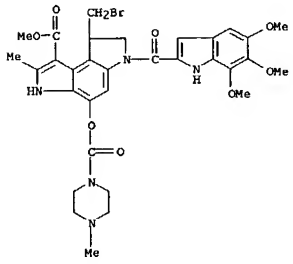
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



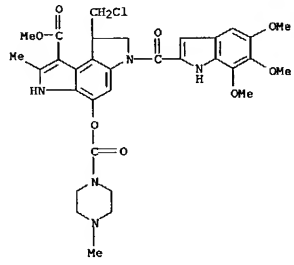
RN 134106-78-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-3,6,7,8-

tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



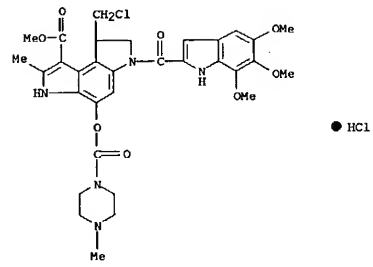
RN 134106-79-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-4-[[(dimethylamino)carbonyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 134106-82-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(chloromethyl)-3,6,7,8-

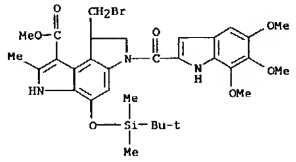
tetrahydro-2-methyl-4-[[(4-methyl-1-piperazinyl)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, monohydrochloride (9CI)
(CA INDEX NAME)



RN 134127-18-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-

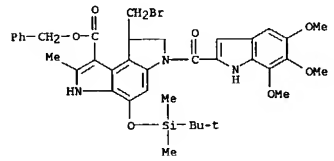
L14 ANSWER 94 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 134127-20-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-

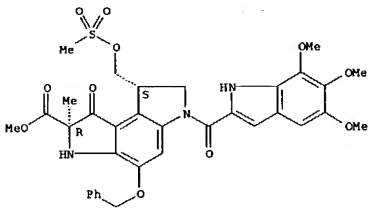
dimethylethyl)dimethylsilyl]oxy]-3,6,7,8-tetrahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

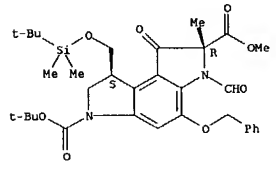
trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



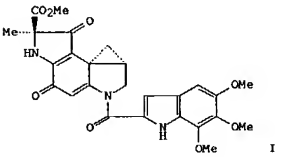
IT **132628-67-2P 132628-68-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrolysis of)
RN 132628-67-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

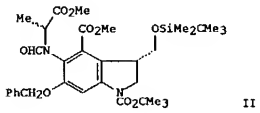


RN 132628-68-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2,6(1H)-dicarboxylic acid, 8-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-3-formyl-2,3,7,8-tetrahydro-2-methyl-1-oxo-4-(phenylmethoxy)-, 6-(1,1-dimethylethyl) 2-methyl ester, cis- (9CI) (CA INDEX NAME)

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:142962 CAPLUS
DN 114:142962
TI First total synthesis of dl-duocarmycin A
AU Fukuda, Yasumichi; Nakatani, Kazuhiko; Ito, Yoshio; Terashima, Shiro
CS Sagami Chem. Res. Cent., Sagamihara, 229, Japan
SO Tetrahedron Letters (1990), 31(46), 6699-702
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 114:142962
GI



I

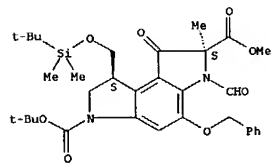


II

AB Synthesis of the title compound (I) was achieved by featuring introduction of a methoxycarbonyl group into the C-4 position of a 5-aminoindoline nucleus by way of an isatin derivative and subsequent ring closure to a Me 2-methylindoxyl-2-carboxylate system by the Dieckmann cyclization the indolylformamide II.
IT **132628-71-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenolysis of)
RN 132628-71-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-2-

methyl-8-[[(methylsulfonyl)oxy]methyl]-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-

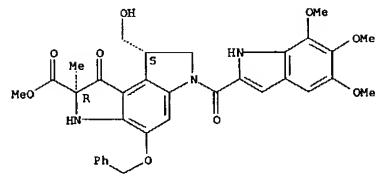
L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Relative stereochemistry.



IT **132628-70-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and mesylation of)
RN 132628-70-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-

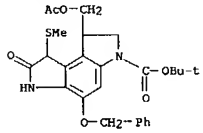
(hydroxymethyl)-2-methyl-1-oxo-4-(phenylmethoxy)-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

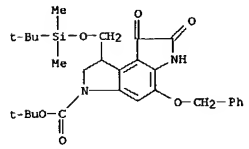


IT **132628-61-6P 132628-63-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and oxidation of)
RN 132628-61-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-
1,6,7,8-tetrahydro-8-(methylthio)-7-oxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

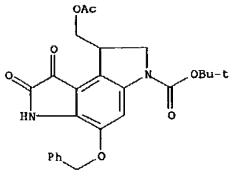


RN 132628-63-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **132628-62-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and silylation of)
RN 132628-62-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[(acetyloxy)methyl]-1,6,7,8-tetrahydro-7,8-dioxo-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 95 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

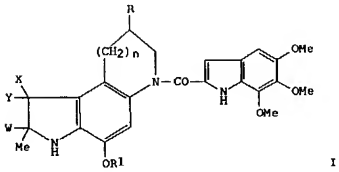


L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

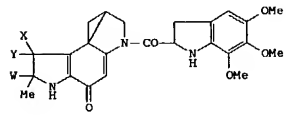
AN 1990:591321 CAPLUS
DN 113:191321
TI Preparation of DC-88A derivatives as antitumor agents
IN Kanda, Yutaka; Yasuzawa, Tohru; Saito, Hiromitsu; Sano, Hiroshi; Kobayashi, Eiji; Morimoto, Makoto
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 365041	A1	19900425	EP 1989-119639	19891023
EP 365041	B1	19951004		
R: DE, FR, GB, IT				
US 5008271	A	19910416	US 1989-423788	19891018
JP 03007287	A2	19910114	JP 1989-272314	19891019
PRAI JP 1988-265582		19881021		
JP 1989-62572		19890315		

OS MARPAT 113:191321
GI



I



II

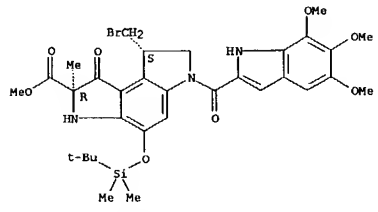
AB DC-88A derivs. [I, II; R = Br, Cl, BrCH2, ClCH2; R1 = H, C1-4 alkyl, C2-15
acyl, (substituted) benzoyl, dialkylcarbamoyl, etc.; one of X and Y is H,
the other is MeO, AcO, (substituted) PhCO2, XY = O; W = H, allyl, (substituted) acyl, alkoxycarbonyl, alkoxymethyl, etc.; n = 0, 1] are

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

prepd. Me3CSiMe2Cl was added to a soln. of DC-89B2 (I; R = BrCH2, R1 = H,
W = CO2Me, XY = O, n = 0) (prepn. by culture fermn. given) and imidazole
in DMF at 0° with stirring, 2N HCl was added, and the mixt. extd. with EtOAc to give 95% silyl ether I (R = BrCH2, R1 = Me3CSiMe2, W = CO2Me, XY = O, n = 0), which showed IC50 of 0.010 nM against HeLa S3 cell
growth, vs. 0.039 nM with DC-88A. Also prepd. were 32 addnl. I and II.

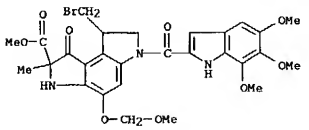
IT **129953-15-7P 129953-16-8P 129953-17-9P**
129953-19-1P 129953-20-4P 129953-21-5P
129953-22-6P 129953-23-7P 129953-24-8P
129953-25-9P 129953-26-0P 129953-28-2P
129953-32-8P 129982-35-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antitumor agent)
RN 129953-15-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R,8S)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



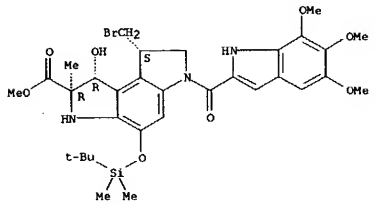
RN 129953-16-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-(methoxymethoxy)-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 129953-17-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-1-hydroxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (1R,2R,8S)-
(9CI) (CA INDEX NAME)

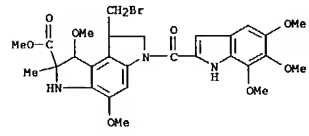
Absolute stereochemistry.



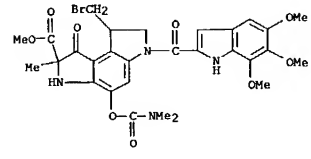
RN 129953-19-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-(acetyloxy)-8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 129953-22-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1,4-dimethoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

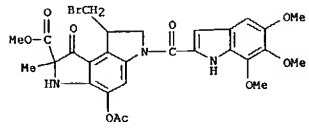


RN 129953-23-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(dimethylamino)carbonyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

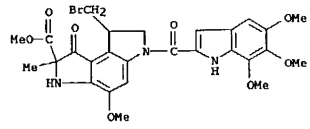


RN 129953-24-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[[(2-propenyloxy)carbonyl]oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

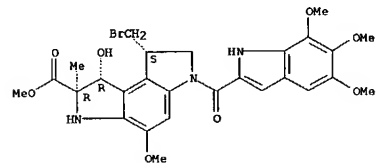


RN 129953-20-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-4-methoxy-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

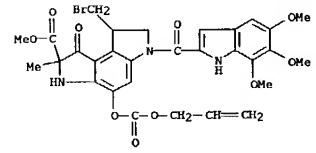


RN 129953-21-5 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-1-hydroxy-4-methoxy-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, [1R-(1α,2β,8α)]-
(9CI) (CA INDEX NAME)

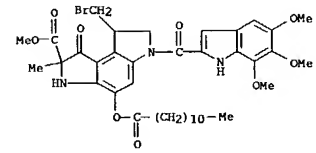
Absolute stereochemistry. Rotation (-).



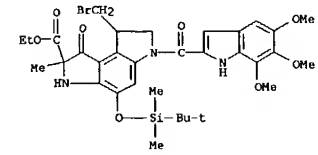
L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 129953-25-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-4-[(1-oxododecyl)oxy]-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

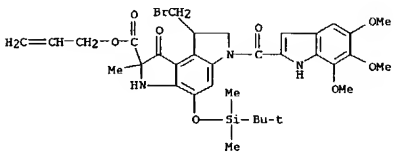


RN 129953-26-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

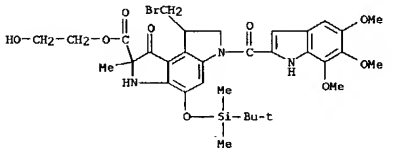


L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 129953-28-2 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

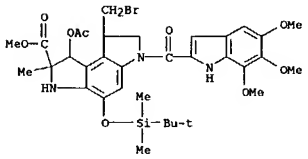


RN 129953-32-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)



RN 129982-35-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1-(acetyloxy)-8-(bromomethyl)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1,2,3,6,7,8-hexahydro-2-methyl-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl

L14 ANSWER 96 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ester (9CI) (CA INDEX NAME)



L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:552387 CAPLUS
DN 113:152387
TI CC-1065 analogs having two CPI subunits useful as antitumor agents and ultraviolet light absorbers
IN Kelly, Robert C.; Aristoff, Paul A.
PA Upjohn Co., USA
SO Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

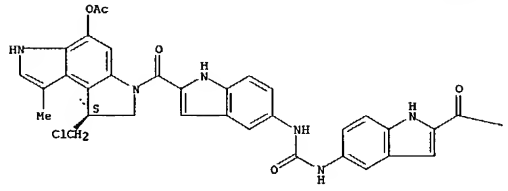
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 359454	A1	19900321	EP 1989-308920	19890904
	EP 359454	B1	20001227		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	WO 9002746	A1	19900322	WO 1989-US3329	19890807
	W: AU, DK, FI, HU, JP, KR, NO, SU, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8941922	A1	19900402	AU 1989-41922	19890807
	AU 632288	B2	19921224		
	JP 04500664	T2	19920206	JP 1989-509236	19890807
	JP 3380237	B2	20030224		
	CA 1340215	A1	19981215	CA 1989-608908	19890821
	AT 198335	E	20010115	AT 1989-308920	19890904
	ES 2153814	T3	20010316	ES 1989-308920	19890904
	KR 137959	B1	19980515	KR 1990-700977	19900511
	DK 9100417	A	19910308	DK 1991-417	19910308
	US 5541339	A	19960730	US 1991-659415	19910308
	NO 9100958	A	19910510	NO 1991-958	19910311
	GR 3035589	T3	20010629	GR 2001-400433	20010315
	LV 12806	B	20020520	LV 2001-180	20011227
PRAI	US 1988-243350	A	19880912		
	WO 1989-US3329	A	19890807		

OS MARPAT 113:152387
GI For diagram(s), see printed CA Issue.
AB CPI1-R5-T-R6-CPI2 [CPI1, CPI2 = Q, Q1; W = alkyl, pH, H; C = N3, halo, cyanato, thiocyanato, isocyanato, thioisocyanato, P(O)(OR)2, etc.; Y = C(O)R, C(S)R, C(O)OE1, C(O)NR2R3, etc.; Z = alkyl, alkenyl, alkynyl, (substituted) Ph, etc.; R1 = alkyl, (substituted) phenyl; R2, R3 = H, alkyl, (substituted) Ph, etc.; T = NHCO, CONH, C(O)O, OC(O), etc.; R5, R6 = bond, acyl etc.], useful as antitumors and UV absorbers in textile industry, were prepared Indole derivative I (R7 = OH) (preparation given) was condensed with benzodipyrrole derivative Q2CO2CMe3 to give I (R7 = Q2). This at 15 μg/kg i.v. effected 60% cure (surviving 30 days) in mice transplanted with L 1210 leukemia cells.
IT **129655-29-4P 129655-34-1P 129655-35-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antitumor and UV absorber)
RN 129655-29-4 CAPLUS

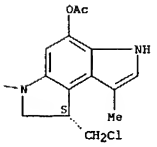
L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Benzo[1,2-b:4,3-b']dipyrrol-4-ol, 6,6'-[carbonylbis(imino-1H-indole-5,2-diylcarbonyl)]bis[8-(chloromethyl)-3,6,7,8-tetrahydro-1-methyl-, diacetate (ester), [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

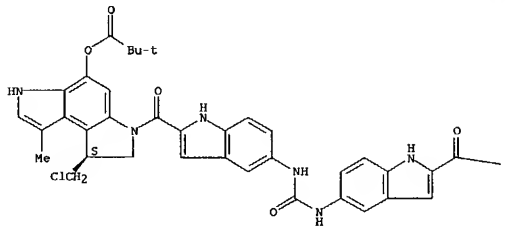


RN 129655-34-1 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, carbonylbis[imino-1H-indole-5,2-diylcarbonyl[1-(chloromethyl)-1,6-dihydro-8-methylbenzo[1,2-b:4,3-b']dipyrrole-3,5(2H)-diyl]] ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

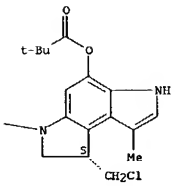
Absolute stereochemistry.

L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

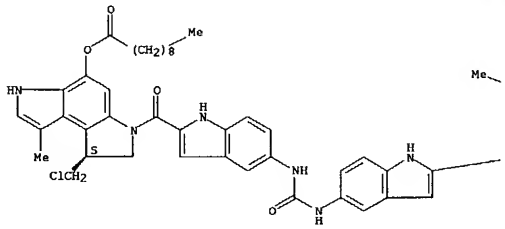


RN 129655-35-2 CAPLUS
CN Decanoic acid, carbonylbis[imino-1H-indole-5,2-diylcarbonyl[1-(chloromethyl)-1,6-dihydro-8-methylbenzo[1,2-b:4,3-b']dipyrrole-3,5(2H)-diyl]] ester, [5-(R*,R*)]- (9CI) (CA INDEX NAME)

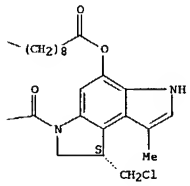
Absolute stereochemistry.

L14 ANSWER 97 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

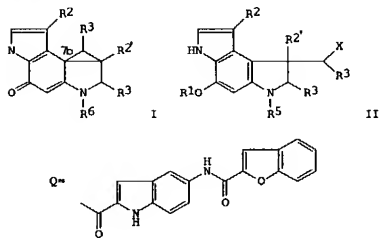


L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:531891 CAPLUS
DN 113:131891
TI Analogs of antibiotic CC-1065, namely 1,2,8,8a-tetrahydrocyclopropa[c]pyrrolo[3,2-e]indol-4-(5H)-ones and related compounds with light-absorbing, antibacterial, and antitumor activities
IN Kelly, Robert C.; Warpehoski, Martha A.; Wierenga, Wendell
PA Upjohn Co., USA
SO U.S., 53 pp. Cont.-in-part of U.S. Ser. No. 694,363, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4912227	A	19900327	US 1986-894314	19860807
	CA 1238907	A1	19880705	CA 1985-473917	19850208
	ZA 8501093	A	19850925	ZA 1985-1093	19850213
	EP 154445	A1	19850911	EP 1985-301125	19850220
	EP 154445	B1	19890531		
	R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
	JP 60193989	A2	19851002	JP 1985-31662	19850221
	JP 2545060	B2	19961016		
	CA 1293248	A2	19911217	CA 1987-552543	19871123
	US 4978757	A	19901218	US 1989-444176	19891130
PRAI	US 1984-581836		19840221		
	US 1985-694363		19850124		
	CA 1985-473917		19850208		
	ZA 1985-1093		19850213		
	EP 1985-301125		19850220		
	JP 1985-31662		19850221		
	US 1986-894314		19860807		
	CA 1987-473917		19870211		

OS MARPAT 113:131891
GI

L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

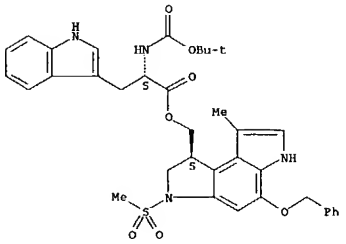


I II

AB Title compds. I and II [R1 = Me, CH2Ph, allyl, CH2SMe, CH2OMe, CH2OCH2CH2OMe, CH2CCl3, CH2CH2Si(R2)3, H; R2, R2', R3 = H, alkyl, Ph; X = Cl, Br, iodo, OSO2R4; R4 = alkyl, Ph, tolyl, C6H4Br, C6H4NO2, CF3; R5 = various carbonyl acyl groups, many containing 1-2 indole and 1-2 amide subunits; R6 = H, R5] were prepared For example, one optical isomer of II (R1 = CH2Ph, R2 = Me, R2' = R3 = H, X = OH, R5 = SO2Me) underwent demesylation, amidation with 5-(2-benzofuranyl carbonylamino)indole-2-carboxylic acid, O-mesylation, conversion to the chloromethyl compound, debenzylation, and cyclization of the chloride to give (7bR, 8aS)-I (R2 = Me, R2' = R3 = H, R6 = acyl group Q) (III). A single i.v. dose of III in mice gave a 61% increase in lifespan after s.c. implantation of B16 melanoma. Fifty synthetic examples and addnl. antitumor results are given.
IT 101151-48-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
RN 101151-48-8 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

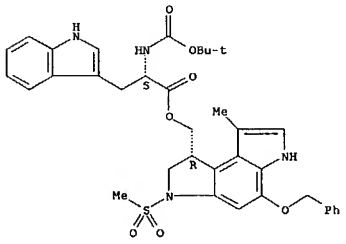
L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **101151-49-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 101151-49-9 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,
[1,2,3,6-tetrahydro-8-

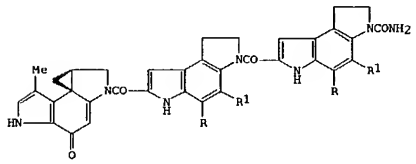
methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

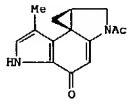


L14 ANSWER 98 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:458759 CAPLUS
DN 113:58759
TI Sequence specificity of DNA alkylation by the unnatural enantiomer of CC-1065 and its synthetic analogs
AU Hurley, Laurence H.; Warpehoski, Martha A.; Lee, Chong Soon; McGovren, J.
Patrick; Scahill, Terrence A.; Kelly, Robert C.; Mitchell, Mark A.; Wicnienski, Nancy A.; Gebhard, Ilse; et al.
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA
SO Journal of the American Chemical Society (1990), 112(12), 4633-49
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 113:58759
GI



I

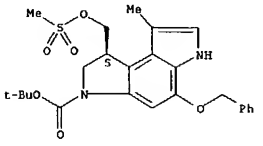


IV

AB (-)-CC-1065, (I, R = OMe, R1 = OH; II), the unnatural enantiomer of the
potent and sequenceselective, DNA-reactive antibiotic, (+)-CC-1065 (III),
was prepared and its covalent reaction with DNA was studied and compared to
that of III. Although II also formed covalent adducts in which the cyclopropyl C was bonded to the N-3 atom of adenine, and the thermal strand breakage that it produced paralleled that seen for III, it lay in
the opposite direction along the minor groove and exhibited a markedly
different sequence requirement for the covalently modified adenine. While

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
II and its analog, (-)-AB'C' (I, R = R1 = H), reacted readily at adenines
near to, but generally distinct from, adenines affected by III, and exhibited potent cytotoxicity, their simpler analogs did not alkylate DNA
under the conditions employed and were biol. nonpotent. At relatively high concns., the smallest such analog, (-)-A, (IV) reacted detectably only at the same sites selected by III. An anal. of the reactivity patterns of II and III and their analogs with DNA restriction fragments
supported the conclusion that the mode of sequence recognition for II adduct formation is fundamentally different from that of III and is primarily controlled by specific minor groove, AT-selective binding interactions, rather than by sequence requirements of the covalent step,
as occurs for III and the (+)-CPI analogs. Models are proposed comparing
the interactions of the enantiomeric alkylating moieties variously oriented in the minor groove at potential reaction sites. The evolutionary significance of both the alkylating moiety and the minor groove binding segments of the natural product is discussed.
IT **110314-49-3P 112836-68-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and chlorination of)
RN 110314-49-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-8-methyl-1-
[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,
(S)- (9CI) (CA INDEX NAME)

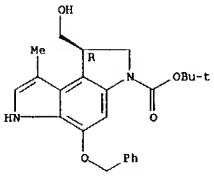
Absolute stereochemistry.



RN 112836-68-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI) (CA INDEX NAME)

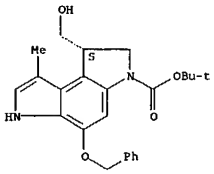
Absolute stereochemistry.

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **112836-67-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and mesylation of)
RN 112836-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) (CA INDEX NAME)

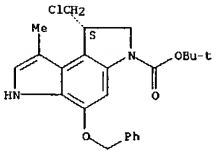
Absolute stereochemistry.



IT **110314-50-6P 112764-69-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reduction of)
RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI)

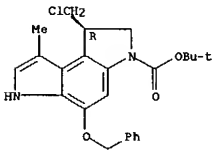
L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



RN 112764-69-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

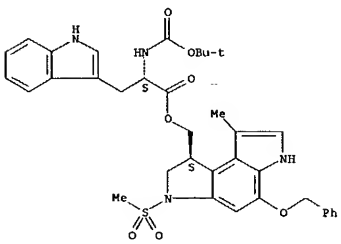


IT **101151-48-8P 101151-49-9P 108859-63-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and saponification of)
RN 101151-48-8 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

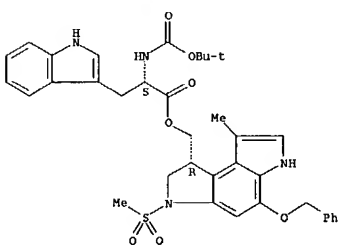
L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 101151-49-9 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

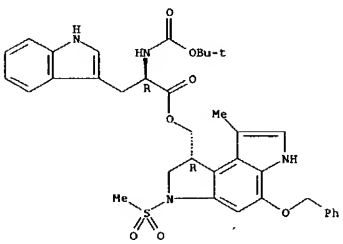


RN 108859-63-8 CAPLUS
CN D-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

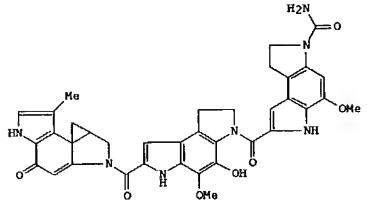
methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 99 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 100 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:400153 CAPLUS
DN 113:153
TI Synthesis and evaluation of aborted and extended CC-1065 functional analogs: (+)- and (-)-CPI-PDE-I1, (+)- and (-)-CPI-CDPI1, and (±)-, (+)-, and (-)-CPI-CDPI3. Preparation of key partial structures and definition of an additional functional role of the CC-1065 central and right-hand subunits
AU Boger, Dale L.; Coleman, Robert S.; Invergo, Benedict J.; Sakya, Subas M.; Ishizaki, Takayoshi; Munk, Stephen A.; Zarrinmayeh, Hamideh; Kitos, Paul A.; Thompson, Sandra Collins
CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
SO Journal of the American Chemical Society (1990), 112(12), 4623-32
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 113:153
GI

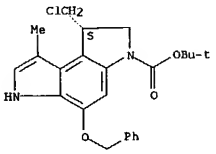


I

AB Aborted and extended analogs of the antitumor antibiotic CC-1065 (NSC 298223) (I) were prepared and tested for in vitro cytotoxicity (L1210 cells) and DNA binding. Covalent alkylation of DNA by the analogs and the structural features required for such action are discussed.
IT **110314-50-6 112764-69-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic hydrogenolysis of, benzyl ether removal by)
RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-(9CI)

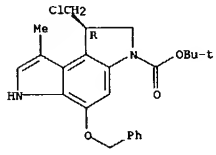
L14 ANSWER 100 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



RN 112764-69-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-(9CI)
(CA INDEX NAME)

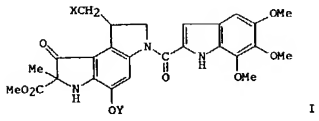
Absolute stereochemistry.



L14 ANSWER 101 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:197974 CAPLUS
DN 112:197974
TI Preparation of antitumor antibiotic SF2582C derivatives
IN Koyama, Masao; Ohba, Kazunori; Nakazawa, Tadashi; Yamamoto, Haruo; Sezaki, Masaji; Kondo, Shinichi
PA Meiji Seika Kaisha, Ltd., Japan
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 339681	A2	19891102	EP 1989-107799	19890428
	EP 339681	A3	19900131		
	EP 339681	B1	19930331		
	R: DE, FR, GB				
	JP 01275581	A2	19891106	JP 1988-103782	19880428
	JP 2562935	B2	19961211		
PRAI	JP 1988-103782		19880428		

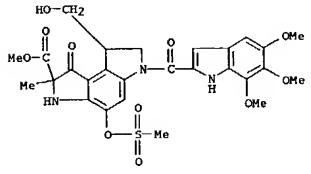
OS MARPAT 112:197974
GI



I

AB Antibiotic SF2582C derivs. (I; X, Y = RSO2; R = tolyl, Me, OH, H; excluding X = Y = X) are prepared, having an intense antitumor activity, while the parent antibiotic SF2582C lacks the antitumor activity. Thus, 40 mg antibiotic SF2582C (II) (isolated from a Streptomyces SF2582 strain) was treated with (MeSO2)2O in DMF containing Et3N to give, after silica gel chromatog., 41 mg I (X = Y = MeSO2) (III) and 6.3 mg II monomethanesulfonate (IV). III and IV increased the life span of mice transplanted with P-388 tumor cells by 54% at 21 mg/kg and 40% at 1 mg/kg, resp.
IT **126590-90-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

L14 ANSWER 101 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(prepn. of, as antitumor agent)
RN 126590-90-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 1,2,3,6,7,8-hexahydro-8-(hydroxymethyl)-2-methyl-4-[(methylsulfonyl)oxy]-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

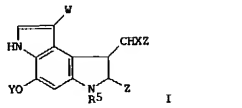


L14 ANSWER 102 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

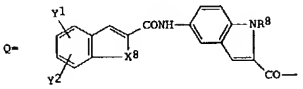
AN 1989:154043 CAPLUS
DN 110:154043
TI Preparation of novel Antibiotic CC 1065 analogs as antitumor agents
IN Kelly, Robert C.; Martin, David G.; Aristoff, Paul A.
PA Upjohn Co., USA
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8804659	A2	19880630	WO 1987-US3227	19871211
	WO 8804659	A3	19880714		
	W: AU, DK, FI, JP, KR, NO, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8812290	A1	19880715	AU 1988-12290	19871211
	AU 617304	B2	19911128		
	EP 340243	A1	19891108	EP 1988-901185	19871211
	EP 340243	B1	19940928		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 02502005	T2	19900705	JP 1988-501400	19871211
	US 5332837	A	19940726	US 1993-10526	19930122
PRAI	US 1986-944633		19861219		
	WO 1987-US3227		19871211		
	US 1989-382159		19890608		
	US 1990-554931		19900718		
	US 1991-674422		19910322		
	US 1992-845762		19920302		

OS MARPAT 110:154043
GI



I



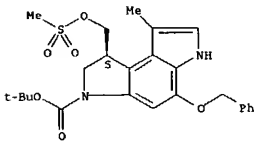
L14 ANSWER 102 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB The title compds. [I; R5 = 22 general acyl and 68 combinations thereof e.g. Q; W, Z = H, alkyl, Ph; X = N3, halo, cyanato, isocyanato, etc.; X8 = O, S, NH; Y = H, COR, CSR, CO2R1, SO2R1, CONR2R3, CSNR2R3, CONHSO2R4; Y1, Y2 = H, halo, alkyl, alkoxy, etc.; R = alkyl, alkenyl, alkynyl, (un)substituted Ph, naphthyl; R1 = alkyl, (un)substituted Ph; R2, R3 = H, alkyl, (un)substituted Ph; R4 = alkyl, (un)substituted Ph, naphthyl; R8 = H, Me, Et] were prepared I (R5 = Q; R8 = Y = Y1 = Y2 = Z = H; W = Me; X = Cl) was stirred 30 min at 5° with AcCl in pyridine to give I (as above except that Y = Ac) which caused a 30-day survival in 4 out 6 mice inoculated with P388 leukemia i.p. at 0.20 mg/kg i.v.

IT **110314-49-3P 110314-50-6P 112836-67-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reaction of, in preparation of antitumor agents)

RN 110314-49-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-8-methyl-1-[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

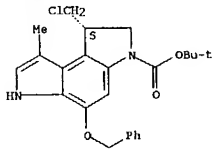
Absolute stereochemistry.



RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

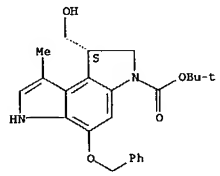
Absolute stereochemistry.

L14 ANSWER 102 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



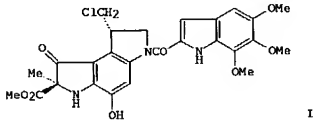
RN 112836-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

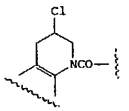


L14 ANSWER 103 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1989:72198 CAPLUS
DN 110:72198
TI Pyrindamycins A and B, new antitumor antibiotics
AU Ohba, Kazunori; Watabe, Hiroomi; Sasaki, Toru; Takeuchi, Yasuo; Kodama, Yoshio; Nakazawa, Tadashi; Yamamoto, Haruo; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi
CS Res. Lab., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan
SO Journal of Antibiotics (1988), 41(10), 1515-19
CODEN: JANTAJ; ISSN: 0021-8820
DT Journal
LA English
GI



I



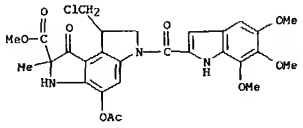
II

AB Pyrindamycins A (I) and B (II) were isolated from the culture broth of Streptomyces sp. SF2582, their structures were determined and they exhibited activity against both gram-pos. and -neg. bacteria. Marked increases in life span were observed with single i.p. treatment of I and II against mice i.p. implanted with P388 leukemia.

IT **118462-85-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 118462-85-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-2-carboxylic acid, 4-(acetyloxy)-8-(chloromethyl)-1,2,3,6,7,8-hexahydro-2-methyl-1-oxo-6-[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]-, methyl ester, (2R-trans)- (9CI) (CA INDEX NAME)

L14 ANSWER 103 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

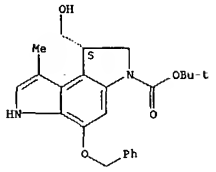


L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:437665 CAPLUS
DN 109:37665
TI Total synthesis of (±)-N2-(phenylsulfonyl)-CPI, (±)-CC-1065, (+)-CC-1065, ent-(-)-CC-1065, and the precise, functional agents (±)-CPI-CDPI2, (+)-CPI-CDPI2, and (-)-CPI-CDPI2 [(±)-(3bR*,4aS*)-, (+)-(3bR,4aS)-, and (-)-(3bS,4aR)-deoxy-CC-1065]
AU Boger, Dale L.; Coleman, Robert S.
CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
SO Journal of the American Chemical Society (1988), 110(14), 4796-807
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 109:37665
AB The title compds. were prepared Left-hand segment is based on the regioselective, nucleophilic addition of 1-piperidino-1-propene to the selectively activated N4-(phenyl)sulfonyl-p-quinone diimide for direct introduction of the 3-methylpyrrole A ring and the subsequent implementation of a 5-exo-dig aryl radical-alkyne cyclization for indirect introduction of the 3-(hydroxymethyl)pyrroline C ring. Spirocyclization gave the spirocyclopropylquinone. CPI-CDPI2 has the structural and *functional features that are responsible for the sequence-selective* B-DNA minor groove association and the potent cytostatic activity of CC-1065. Both CC-1065 and CPI-CDPI2 constitute reactive alkylating agents superimposed on the CDPI trimer skeleton and derive their B-DNA associating properties through hydrophobic binding-driven bonding. It is predominantly hydrophobic interactions of the concave face of CC-1065 and its B-DNA minor-groove complementary shape that permit the association with AT-rich minor-groove regions and promote the irreversible adenine N-3 covalent alkylation.
IT **112836-67-6P 112836-68-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)
RN 112836-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) *(CA INDEX NAME)*

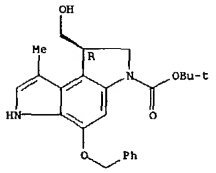
Absolute stereochemistry.

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112836-68-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI) (CA INDEX NAME)

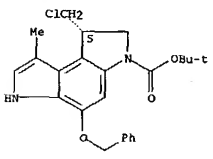
Absolute stereochemistry.



IT **110314-50-6P 112764-69-9P 175614-07-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and debenzylation of)
RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-(9CI)
(CA INDEX NAME)

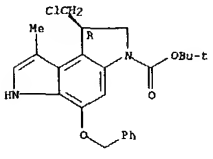
Absolute stereochemistry.

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

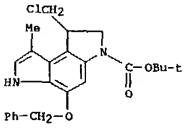


RN 112764-69-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



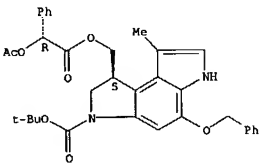
RN 175614-07-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **112764-68-8P 112793-57-4P**

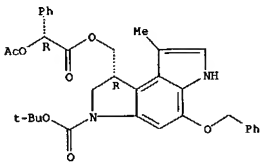
L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and ester hydrolysis of)
RN 112764-68-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



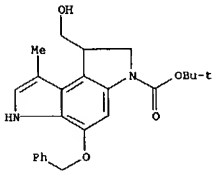
RN 112793-57-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

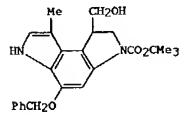


IT **112089-71-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)

L14 ANSWER 104 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(prepn. and resoln. of)
RN 112089-71-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

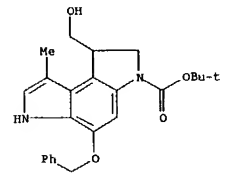


L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:437661 CAPLUS
DN 109:37661
TI Total synthesis of (+)- and (-)-CPI-CDPI2: (+)-(3bR,4aS)- and (-)-(3bS,4aR)-deoxy-CC-1065
AU Boger, Dale L.; Coleman, Robert S.
CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
SO Journal of Organic Chemistry (1988), 53(3), 695-8
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
OS CASREACT 109:37661
GI



II

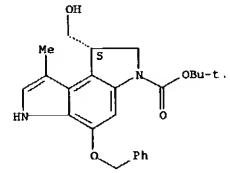
AB The title compds. [(+)- and (-)-I] were obtained in high enantiomeric purity by a sequence involving resolution of the intermediate II via an optically active ester. (+)-I and (-)-I have antitumor ED50 of 3.9 + 10-6 and 1.2 + 10-5 μg/mL, resp., against P388 leukemia.
IT **112089-71-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification with, of optically active carboxylic acids)
RN 112089-71-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)



IT **112836-67-6P 112836-68-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

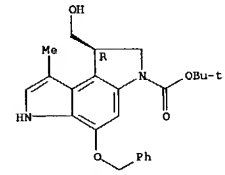
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Reactant or reagent)
(prepn. and chlorination of)
RN 112836-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 112836-68-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI) (CA INDEX NAME)

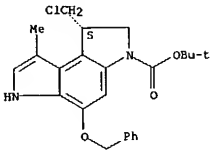
Absolute stereochemistry.



IT **110314-50-6P 112764-69-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and deblocking of)
RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI)

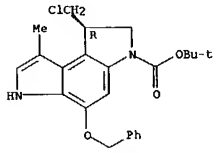
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(CA INDEX NAME)

Absolute stereochemistry.



RN 112764-69-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,
1-(chloromethyl)-1,6-
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI)
(CA INDEX NAME)

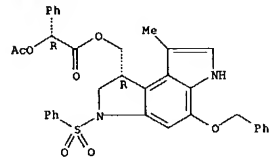
Absolute stereochemistry.



IT **112764-68-8P 112793-57-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(preparation and ester hydrolysis of)
RN 112764-68-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-
[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-
(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,S*)]- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

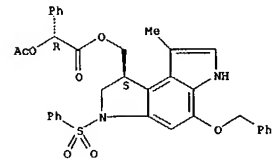
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 114928-10-8 CAPLUS
CN Benzeneacetic acid, α-(acetyloxy)-, [1,2,3,6-tetrahydro-8-methyl-5-

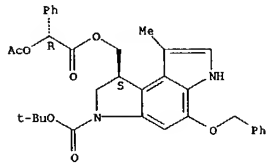
(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl
ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



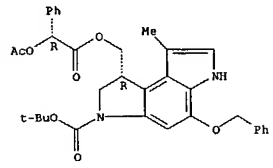
RN 114928-11-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,
1,6-dihydro-8-methyl-1-
[[[[[5-methyl-2-(1-methylethyl)cyclohexyl]oxy]acetyl]oxy]methyl]-5-
(phenylmethoxy)-, 1,1-dimethylethyl ester, [1R-
[1α(R*),2β,5α]]- (9CI) (CA INDEX NAME)

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112793-57-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-
[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-
(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,R*)]- (9CI) (CA
INDEX
NAME)

Absolute stereochemistry.

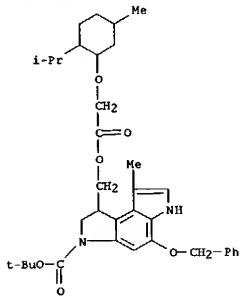


IT **114928-09-5P 114928-10-8P 114928-11-9P**
114928-12-0P 114928-13-1P 114928-14-2P
114928-15-3P 114928-16-4P 114928-17-5P
114928-18-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 114928-09-5 CAPLUS
CN Benzeneacetic acid, α-(acetyloxy)-, [1,2,3,6-tetrahydro-8-methyl-5-

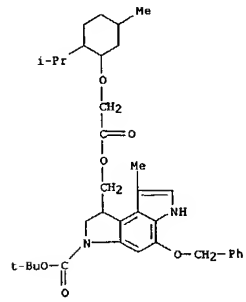
(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl
ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 114928-12-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,
1,6-dihydro-8-methyl-1-
[[[[[5-methyl-2-(1-methylethyl)cyclohexyl]oxy]acetyl]oxy]methyl]-5-
(phenylmethoxy)-, 1,1-dimethylethyl ester, [1R-
[1α(S*),2β,5α]]- (9CI) (CA INDEX NAME)

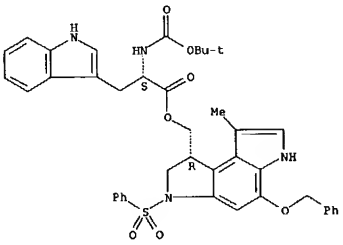


RN 114928-13-1 CAPLUS

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,
[1,2,3,6-tetrahydro-8-

methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

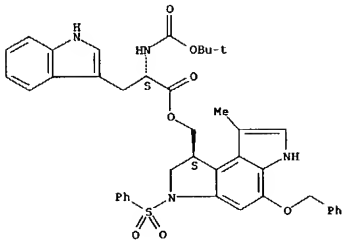


RN 114928-14-2 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-,
[1,2,3,6-tetrahydro-8-

methyl-5-(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

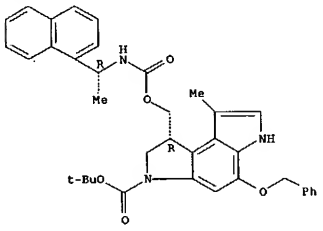
L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 114928-15-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,
1,6-dihydro-8-methyl-1-

[[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]oxy]methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

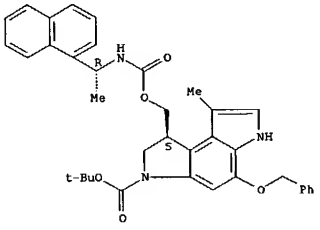


RN 114928-16-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid,
1,6-dihydro-8-methyl-1-

[[[[[1-(1-naphthalenyl)ethyl]amino]carbonyl]oxy]methyl]-5-(phenylmethoxy)-

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
, 1,1-dimethylethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

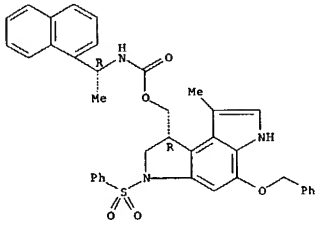
Absolute stereochemistry.



RN 114928-17-5 CAPLUS
CN Carbamic acid, [1-(1-naphthalenyl)ethyl]-,
[1,2,3,6-tetrahydro-8-methyl-5-

(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

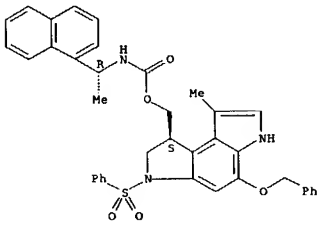
Absolute stereochemistry.



RN 114928-18-6 CAPLUS
CN Carbamic acid, [1-(1-naphthalenyl)ethyl]-,
[1,2,3,6-tetrahydro-8-methyl-5-

(phenylmethoxy)-3-(phenylsulfonyl)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

L14 ANSWER 105 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.



L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:112038 CAPLUS
DN 108:112038
TI Total synthesis of (+)-CC-1065 and ent-(-)-CC-1065
AU Boger, Dale L.; Coleman, Robert S.
CS Dep. Chem., Purdue Univ., West Lafayette, IN, 47907, USA
SO Journal of the American Chemical Society (1988), 110(4), 1321-3
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 108:112038
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

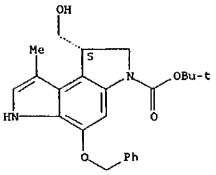
AB The spirobicyclo[5.2.0]octa-2,5-dien-4-one left-hand segment I of CC-1065
was prepared and its immediate precursor II resolved and coupled with synthetic PDE-I dimer in the total syntheses of natural (+)-CC-1065 (III)
and unnatural ent-(-)-CC-1065. The approach to I is based on the regioselective, nucleophilic addition of 1-piperidino-1-propene to a selectively activated N4-benzenesulfonyl p-quinonediimide for direct, 3-methylpyrrole introduction, implementation of a 5-exo-dig aryl radical-alkyne cyclization for indirect 3-hydroxymethylindoline introduction and resolution of II. The Winstein Ar-3' cyclization was used
for final introduction of the reactive, electrophilic spirocyclopropane.
III and its isomer have the same antitumor activity.

IT **112836-67-6P 112836-68-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and chlorination of)

RN 112836-67-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI) (CA INDEX NAME)

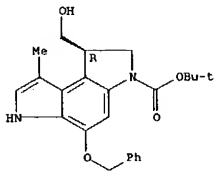
Absolute stereochemistry.

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112836-68-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

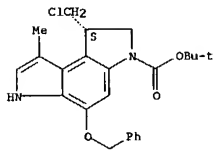


IT **110314-50-6P 112764-69-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and deblocking of)

RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)-
(9CI)
(CA INDEX NAME)

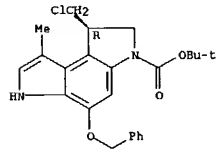
Absolute stereochemistry.

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112764-69-9 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (R)-
(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

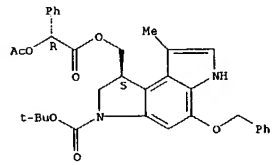


IT **112764-68-8P 112793-57-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and ester hydrolysis of)

RN 112764-68-8 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX
NAME)

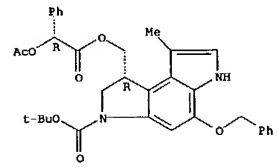
Absolute stereochemistry.

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 112793-57-4 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-[[[(acetyloxy)phenylacetyl]oxy]methyl]-1,6-dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, [R-(R*,R*)]- (9CI) (CA INDEX
NAME)

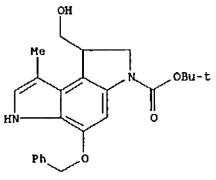
Absolute stereochemistry.



IT **112089-71-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and esterification of)

RN 112089-71-1 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester
(9CI)
(CA INDEX NAME)

L14 ANSWER 106 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 107 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1988:94431 CAPLUS

DN 108:94431

TI Stereoelectronic factors influencing the biological activity and DNA interaction of synthetic antitumor agents modeled on CC-1065

AU Warpehoski, M. A.; Gebhard, I.; Kelly, R. C.; Krueger, W. C.; Li, L. H.; McGovren, J. P.; Prairie, M. D.; Wicnienski, N.; Wierenga, W.

CS Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA

SO Journal of Medicinal Chemistry (1988), 31(3), 590-603
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

OS CASREACT 108:94431

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

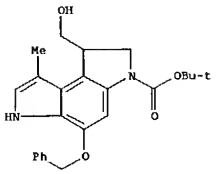
AB The synthesis, physicochem. properties, and biol. activities of 21 novel spiro cyclopropyl compds., e.g. I [R = H, SO2Ph, CO2CMe3, COMe, substituted (indol-2-yl)carbonyl], prepared by intramol. cyclopropanation of pyrroloindoles II (R1 = PhCH2, R2 = SO2CF3; R1 = R2 = H), are described. Many I are more effective than the antitumor antibiotic CC-1065 (III) against murine tumors. In particular, IV exhibits high activity and potency. Structure-activity anal. supports a mol. mechanism of biol. action involving hydrophobic interaction of the drug with DNA and acid-catalyzed alkylation of DNA.

IT **112089-71-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 112089-71-1 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-1-(hydroxymethyl)-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester (9CI)
(CA INDEX NAME)

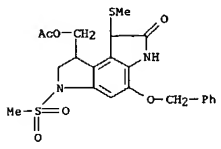
L14 ANSWER 107 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **112089-53-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of, stereochem. of)

RN 112089-53-9 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-6-(methylsulfonyl)-1-(methylthio)-4-(phenylmethoxy)- (9CI) (CA INDEX NAME)

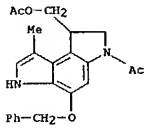


IT **112089-75-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

RN 112089-75-5 CAPLUS

CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 3-acetyl-1,2,3,6-tetrahydro-8-methyl-5-(phenylmethoxy)-, acetate (ester) (9CI) (CA INDEX NAME)

L14 ANSWER 107 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



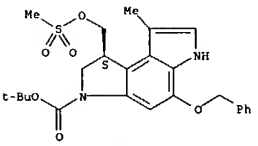
L14 ANSWER 108 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:597901 CAPLUS
DN 107:197901
TI Coupling of cyclopropapyrroloindole (CPI) derivatives. The preparation of
CC-1065, ent-CC-1065, and analogs
AU Kelly, Robert C.; Gebhard, Ilse; Wicnienski, Nancy; Aristoff, Paul A.;
Johnson, Paul D.; Martin, David G.
CS Cancer and Viral Dis. Res., Upjohn Co., Kalamazoo, MI, 49001, USA
SO Journal of the American Chemical Society (1987), 109(22), 6837-8
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
OS CASREACT 107:197901
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB CC-1065 (I, R = R1) and its analogs I (R = pentyl, 2-indolyl, R2, X = NH,
O) were prepared from the pyrroloindole II (R3 = OH, R4 = H, R5 = CH2Ph) via
II (R3 = Cl, R4 = CO2CMe3, R5 = H), II (R3 = Cl, R4 = R5 = H), and II (R3
= Cl, R4 = COR, R5 = H). Ent-CC-1065 was similarly prepared and had an ED50
against leukemia L1210 of 4.5 + 10-12 g/mL.
IT **110314-49-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and chlorination of)
RN 110314-49-3 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1,6-dihydro-8-methyl-1-
[[(methylsulfonyl)oxy]methyl]-5-(phenylmethoxy)-, 1,1-dimethylethyl ester,
(S)- (9CI) (CA INDEX NAME)

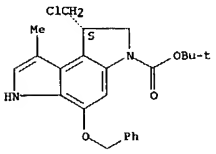
Absolute stereochemistry.

L14 ANSWER 108 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

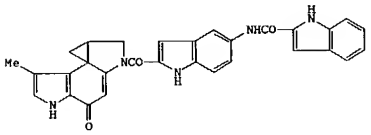


IT **110314-50-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and hydrogenolysis of)
RN 110314-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-3(2H)-carboxylic acid, 1-(chloromethyl)-1,6-
dihydro-8-methyl-5-(phenylmethoxy)-, 1,1-dimethylethyl ester, (S)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 109 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:423139 CAPLUS
DN 107:23139
TI Total synthesis of U-71184, a potent new antitumor agent modeled on CC-1065
AU Warpehoski, M. A.
CS Upjohn Co., Kalamazoo, MI, 49001, USA
SO Tetrahedron Letters (1986), 27(35), 4103-6
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 107:23139
GI



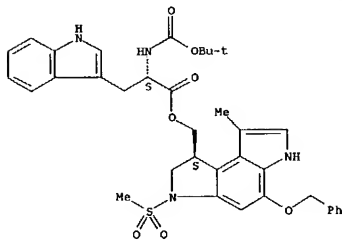
I

AB U-71184 (I), a highly potent analog of novel antitumor antibiotic CC-1065,
involves the unmasking of a p-hydroxyphenethyl mesylate, which undergoes
facile intramol. elimination to afford the reactive cyclopropylspirocyclohexadienone. Its enantiomer, U-71185, was also prepared I had antitumor activity comparable to that of CC-1065 without the
delayed toxicity, but U-71185 was inactive.
IT **101151-48-8P 108859-63-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and saponification of)
RN 101151-48-8 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

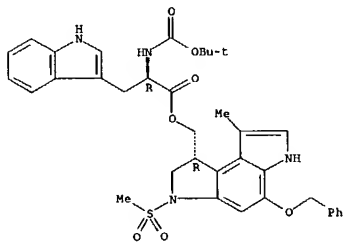
L14 ANSWER 109 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 108859-63-8 CAPLUS
CN D-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

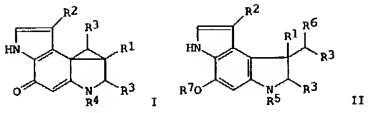
Absolute stereochemistry.



L14 ANSWER 110 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1986:148641 CAPLUS
DN 104:148641
TI Analogs of antibiotic CC-1065
IN Kelly, Robert Charles; Warpehoski, Martha Ann; Wierenga, Wendell
PA Upjohn Co. , USA
SO Eur. Pat. Appl., 96 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 154445	A1	19850911	EP 1985-301125	19850220
	EP 154445	B1	19890531		
	R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
	US 4912227	A	19900327	US 1986-894314	19860807
	JP 08225573	A2	19960903	JP 1995-331640	19951220
PRAI	US 1984-581836		19840221		
	US 1985-694363		19850124		
	CA 1985-473917		19850208		
	ZA 1985-1093		19850213		
	EP 1985-301125		19850220		
	JP 1985-31662		19850221		

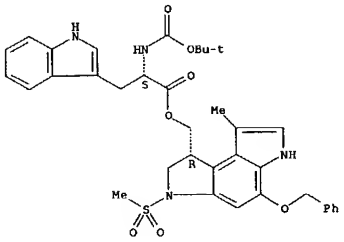
GI



I II

AB Title compds. I and II (R1, R2, R3 = H, alkyl, phenyl; R4 = H, acyl; R5 = acyl; R6 = halo, substituted sulfonyloxy; R7 = Me, substituted Me) and their salts, useful as UV light absorbants, bactericides, and antitumors were prepared Thus, II (R1 = R2 = R3 = H, R5 = mesyl, R7 = PhCH2) was N-demesylated, N-acetylated, O-mesylated, O-debenzylated, and cyclized to give I (R1 = R2 = R3 = H, R4 = Ac). The latter compound showed cytotoxic activity against murine L1210 tumor cells at 0.0048 μg/mL.
IT **101151-48-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

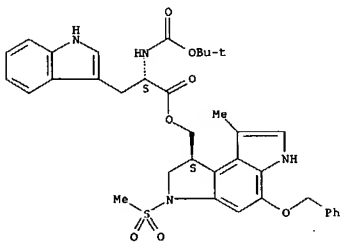
L14 ANSWER 110 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L14 ANSWER 110 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Reactant or reagent)
(prepn. and hydrolysis of)
RN 101151-48-8 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **101151-49-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 101151-49-9 CAPLUS
CN L-Tryptophan, N-[(1,1-dimethylethoxy)carbonyl]-, [1,2,3,6-tetrahydro-8-

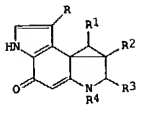
methyl-3-(methylsulfonyl)-5-(phenylmethoxy)benzo[1,2-b:4,3-b']dipyrrol-1-yl]methyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L14 ANSWER 111 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1984:156432 CAPLUS
DN 100:156432
TI 1,2,8,8A-Cyclopropa[c]benzo[1,2,-b:-4,3-b']dipyrrol-4(5H)-ones
IN Wierenga, Wendell
PA Upjohn Co. , USA
SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 207,838, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4424365	A	19840103	US 1982-391055	19820622
	DE 3142143	A1	19820624	DE 1981-3142143	19811023
	DE 3142143	C2	19920730		
	DE 3153725	C2	19930318	DE 1981-3153725	19811023
	CH 655726	A	19860515	CH 1981-4003	19811028
	CH 655724	A	19860515	CH 1981-6895	19811028
	FR 2494273	A1	19820521	FR 1981-21480	19811117
	FR 2494273	B1	19851220		
	JP 57114589	A2	19820716	JP 1981-183170	19811117
	JP 03010629	B4	19910214		
	SU 1318165	A3	19870615	SU 1981-3353089	19811117
	US 4400518	A	19830823	US 1982-346465	19820208
	US 4413132	A	19831101	US 1982-346463	19820208
	US 4423230	A	19831227	US 1982-346459	19820208
	US 4423228	A	19831227	US 1982-346460	19820208
	US 4423229	A	19831227	US 1982-346461	19820208
	US 4431820	A	19840214	US 1982-346464	19820208
	US 4496492	A	19850129	US 1983-515434	19830719
	JP 03014581	A2	19910123	JP 1990-134241	19900525
	JP 04065076	B4	19921016		
	JP 03014545	A2	19910123	JP 1990-134242	19900525
	JP 04060594	B4	19920928		
	JP 03014561	A2	19910123	JP 1990-134243	19900525
	JP 04027231	B4	19920511		
PRAI	US 1980-207838		19801118		
	CH 1981-6895		19811028		
	US 1982-346642		19820208		

OS CASREACT 100:156432
GI

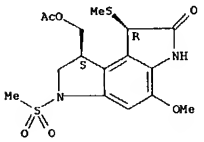


I

AB The title compds. I (R-R3 = H, alkyl, Ph; R4 = SO2R5, CO2CH2R6; R5 = H,

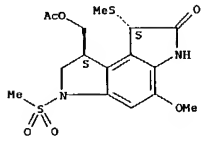
L14 ANSWER 111 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
alkyl, Ph, CH2COPh; R6 = CH2I, CCl3, CH2SO2R5, Ph, fluorenylmethyl) were
prepd. Thus, I [R = Me, R1-R3 = H, R4 = SO2Me (II)] was prepd. from 2,5-O2N(MeO)C6H3CH(CO2Et)2 in 10 steps. II is a fragment of antibiotic
CC-1065 and has an ED50 against leukemia L1210 in vitro of 0.13 μg/mL.
II also has bactericidal activity (no data).
IT **140862-50-6P 140862-51-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and reduction of)
RN 140862-50-6 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, cis- (9CI) (CA
INDEX NAME)

Relative stereochemistry.

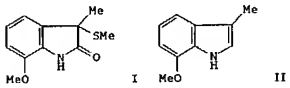


RN 140862-51-7 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrol-2(1H)-one, 8-[(acetyloxy)methyl]-3,6,7,8-tetrahydro-4-methoxy-6-(methylsulfonyl)-1-(methylthio)-, trans- (9CI) (CA
INDEX NAME)

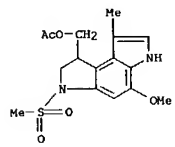
Relative stereochemistry.



L14 ANSWER 112 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:505087 CAPLUS
DN 99:105087
TI A versatile and efficient process to 3-substituted indoles from anilines
AU Wierenga, Wendell; Griffin, John; Warpehoski, Martha A.
CS Cancer Res., Upjohn Co., Kalamazoo, MI, 49001, USA
SO Tetrahedron Letters (1983), 24(24), 2437-40
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 99:105087
GI



AB Borane-mediated reductive elimination of α-methylthio-, α-hydroxy-, or α-alkoxy-α1-substituted oxindoles affords 3-substituted indoles in high yield. Thus, treating oxindole I with Me2S·BH3 or tetrahydrofuran·BH3 gave 92% indole II.
IT **86915-20-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 86915-20-0 CAPLUS
CN Benzo[1,2-b:4,3-b']dipyrrole-1-methanol, 1,2,3,6-tetrahydro-5-methoxy-8-methyl-3-(methylsulfonyl)-, acetate (ester) (9CI) (CA INDEX NAME)



L14 ANSWER 111 OF 112 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)